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DIAPHRAGMATIC HERNIA IN INFANTS

REPORT OF TWO CASES

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Congenital hernia of the diaphragm may be encountered at any stage of life and may attain a considerable size without becoming incompatible with fairly good health. It is seen frequently in the newborn and occasionally in the aged. Few infants, however, live long if obstructive symptoms develop, and most of them die within a few hours or at most a few days after birth. Furthermore, successful operative results in infants under 1 year of age are few, as may be seen from the report of Orr,[1] who in a careful survey of the literature up to 1936 found records of only 17 infants who had been operated on and of only 8 who had survived the surgical procedure.[2] One cannot read the details

From the Presbyterian Hospital.

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2. McCleave, T. C.: Diaphragmatic Hernia, Am. J. Dis. Child. **13**:252 (March) 1917. DeBuys, L. R.: A Case of Anomaly of the Diaphragm, with Herniation into the Thorax of Certain Viscera Resulting in a Gastric and Intestinal Obstruction, ibid. **19**:55 (Jan.) 1920. Barnett, G. S.: Congenital Deficiency of the Diaphragm, Brit. M. J. **1**:602, 1921. Woolsey, J. H.: Diaphragmatic Hernia, J. A. M. A. **89**:2245 (Dec. 31) 1927. Olmsted, H. C.: Nontraumatic Lesions of the Diaphragm in Infancy and Childhood, Northwest Med. **27**:169, 1928. Meyer, W., in discussion on Harrington, S. W.: Diaphragmatic Hernia, Arch. Surg. **16**: 386 (Jan., pt. 2) 1928. Bettman, R. B., and Hess, J. H.: Incarcerated Diaphragmatic Hernia in an Infant, with Operation and Recovery, J. A. M. A. **92**:2014 (June 15) 1929. Donovan, E. J.: Repair of Diaphragmatic Hernia in an Infant, S. Clin. North America **11**:517, 1931. Bettman, R., and Hess, J.: Diaphragmatic Hernia in an Infant, Ann. Surg. **93**:1274, 1931. Eggers, C.: Hernia or Eventration of the Diaphragm, J. Thoracic Surg. **1**:41, 1931. Robb, E. F.: Congenital Diaphragmatic Hernia: Successful Result, Journal-Lancet **51**:

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of these reports without coming to the conclusion that the high mortality is due to the difficulty in making an early diagnosis, the trouble encountered in preparation of the baby for the operation and the technical difficulties incident to the operative procedure itself. In our limited personal experience two extremes have been met with: (1) a case in which the diagnosis was easy (being almost self evident on inspection), the problem of preoperative preparation comparatively simple, the surgical procedure involved in reduction of the abnormal contents of the thoracic cavity and repair of the defect in the diaphragm not difficult and the outcome successful, and (2) a case in which the diagnosis was impossible without roentgen examination, the preparation of the baby for the operation extremely difficult and the final outcome, after three major operations, fatal.

REPORT OF CASES

CASE 1.—R. M., a boy aged 3 months, was admitted to the Presbyterian Hospital on July 24, 1935, to the service of Dr. A. H. Parmelee, with the following history: Delivery (April 20) had been normal; the weight at birth was 8 pounds 10 ounces (3,705 Gm.). He had never been breast fed and had been given several formulas without much success. At 7 weeks of age he began to vomit and the stools became loose, conditions which persisted in spite of every effort to modify his food. During the past ten days sweetened condensed milk had been used, and the vomiting had been much less. On entrance to the hospital, examination revealed a thin baby weighing 10 pounds (4,535 Gm.). The skin was covered by a heat rash. The length was 25 inches (63.5 cm.). The chest seemed unusually prominent and the abdomen unusually flat. The area of cardiac dulness was well to the right of the sternum, and the tones were heard best in this area. Over the left side of the thorax a tympanitic note was elicited on percussion, breath sounds were indistinct, and some gurgling noises were heard with the stethoscope. The diagnosis of diaphragmatic hernia on the left was, of course, readily made. Under the fluoroscope, by plain roentgenograms and by oral administration of barium sulfate this impression was easily confirmed (fig. 1) by Dr. F. H. Squire, who reported: "The heart shadow is displaced to the right. The entire left lung field is crowded by rounded masses of decreased density, giving an exaggerated honeycomb appearance, which is more or less characteristic of air in the small bowel. There is good excursion of the diaphragm, the left side of which moves in the opposite direction (paradoxically). Barium readily enters and fills the stomach, which is rather large and lies in its normal position in the abdomen. One-half hour later barium is seen in the small bowel, many loops of which have passed through a lateral defect in the diaphragm and have occupied the entire left pleural cavity" (fig. 2).

In preparation of the baby for the surgical operation Dr. Parmelee encountered relatively little trouble. The infant was fed mostly by gavage because of cyanosis

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517, 1931. Johnson, H., and Bower, A. G.: Strangulated Diaphragmatic Hernia in an Infant, California & West. Med. **36**:48, 1932. Unshelm, E.: Hernia hiatus aesophagie beim Kind, Monatschr. f. Kinderh. **51**:94, 1931. Barrett, N. R., and Wheaton, C. E. W.: Pathology, Diagnosis and Treatment of Congenital Diaphragmatic Hernia in Infants, Brit. J. Surg. **21**:420, 1934. Coryllos, A. N.: Two Cases of Diaphragmatic Hernia, S. Clin. North America **14**:285, 1934. Iizuka, F., and Sano, U.: Angeborene Zwerchfellhernie beim Säugling (mit Erfolg operierter Fall), Orient. J. Dis. Infants **11**:23, 1932.

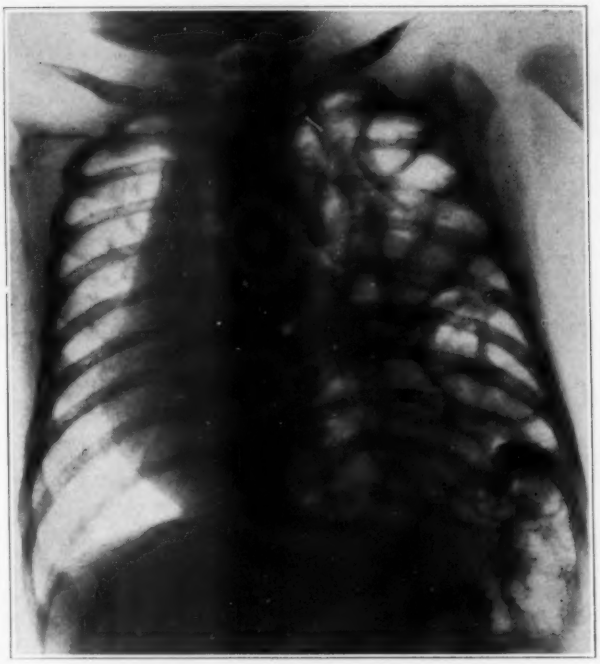

Fig. 1 (case 1).—R. M., aged 3½ months, with a diaphragmatic hernia on the left. The roentgenogram shows the appearance of the left side of the chest before the introduction of barium sulfate by mouth.

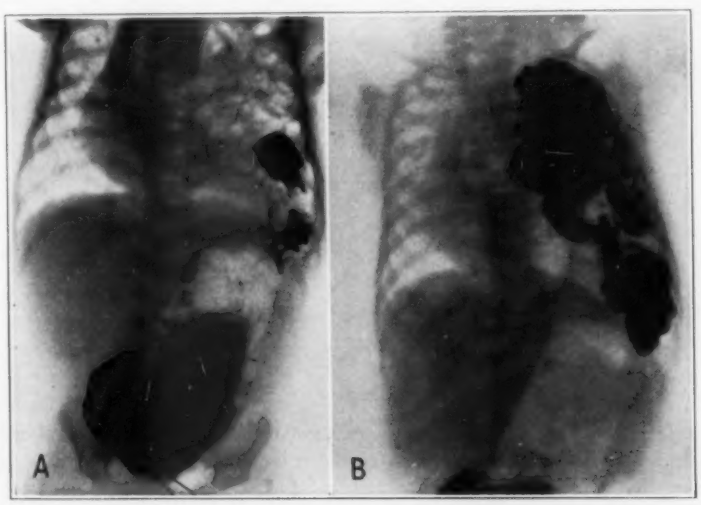

Fig. 2 (case 1).—*A*, portion of the defect in the diaphragm, close to the chest wall. The stomach occupies a normal position. *B*, barium-filled loops of bowel occupying the left pleural cavity.

and choking when the dropper was used. Progress was satisfactory, and by August 1 (eight days after admission) he had gained 3½ ounces (99 Gm.). The next day, however, he showed a drop in weight, and it was decided that further delay in operating was unwise. The blood count showed: hemoglobin, 80 per cent; red cells, 4,850,000; white cells, 9,500. On August 2, therefore, after a blood transfusion of 90 cc. had been given intravenously by scalp vein, operation was performed (by Dr. Miller). In view of the experience of other surgeons with similar problems, the combined thoracic and abdominal approach seemed logical. With the child under ether anesthesia the abdomen was opened through an oblique incision parallel to the costal border on the left. The left side of

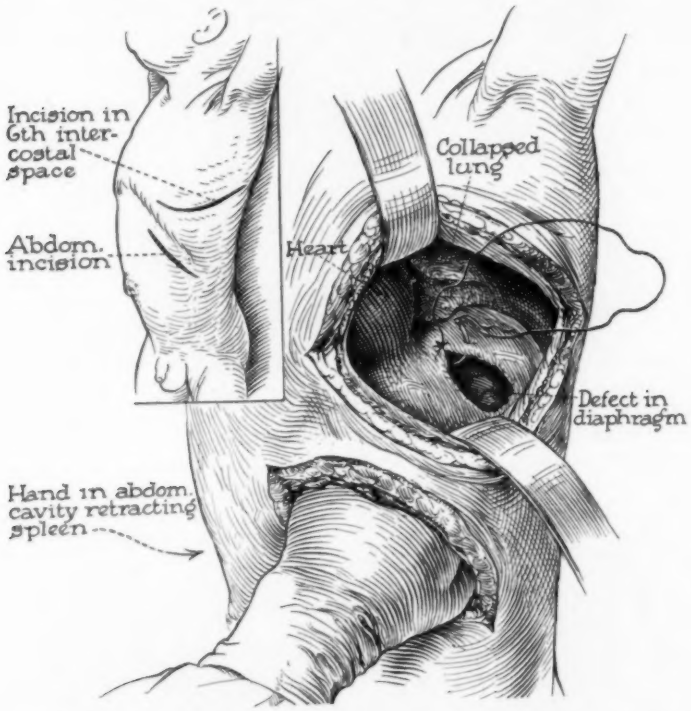

Fig. 3 (case 1).—Method of closure of the defect in the left side of the diaphragm after reduction of the small bowel and the colon into the abdomen.

the chest was then opened by a long incision through the sixth interspace, and the margins were widely retracted. There was, of course, no need for positive pressure anesthesia, because the lung on this side had long since been collapsed. The left side of the chest was completely filled with loops of small bowel; most of the colon was also present. The cecum and appendix lay near the apex of the cavity. The heart was pushed markedly to the right, and beyond it, through the mediastinal pleura, could be seen the pink, aerated right lung, working easily. The collapsed left lung could be recognized as a small purple mass at the hilus. In order to reduce the displaced loops of bowel through the defect in the diaphragm, it was necessary for the surgeon to introduce his left hand into the abdomen and spread the opening with two fingers while with the right hand he gently pushed first the colon and then the loops of small bowel through the

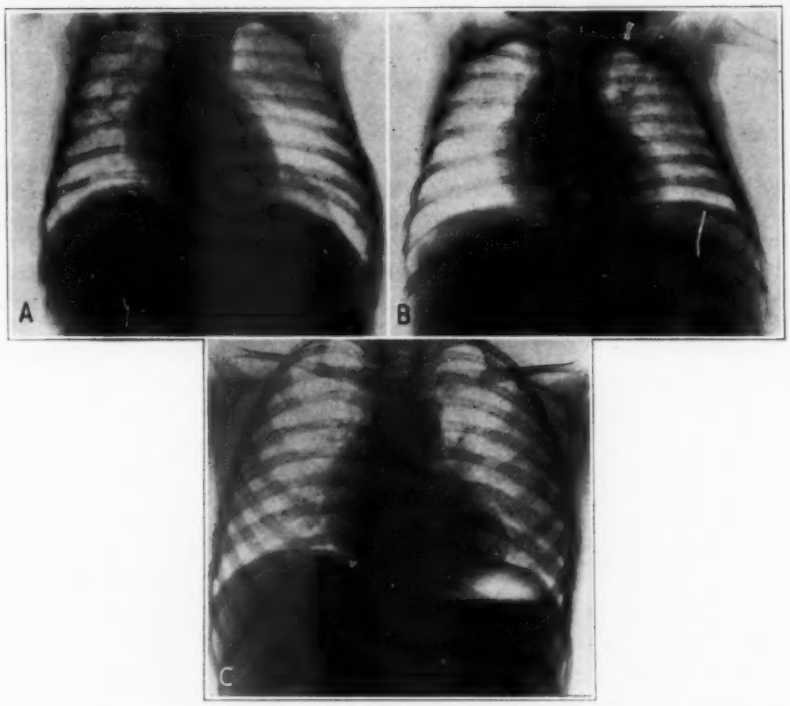

Fig. 4 (case 1).—*A*, roentgen appearance of the chest one day after the operation. Note the air partly filling the left pleural cavity. *B*, appearance of the chest three weeks after the operation. Note the complete expansion of the left lung and the normal curve of the diaphragm. *C*, roentgenogram taken two years and eight months after the operation.

Fig. 5 (case 1).—Photograph of R. M., taken two years and eight months after the operation.

opening. The spleen was the organ which interfered most with this maneuver, as it lay snugly in the defect. The defect was trianglar, its base being against the lateral wall of the chest and each side being about 2½ inches (6.2 cm.) long. Repair was easily made from the thoracic side (fig. 3); a running catgut suture was used, which effectively brought the sides of the defect together without tension. The long opening in the wall of the chest was then quickly closed after interrupted catgut sutures had been placed around the adjacent ribs and fine catgut in the margins of the intercostal muscles. The several loops of intestine, which during this closure had been kept warm with pads, were gently reduced within the abdomen, and the incision was brought together in the usual way.

The postoperative course was remarkably uneventful. Small feedings of breast milk were quickly resumed by gavage and were well taken. Breathing became easier and more regular. Roentgenograms of the chest, taken on the following day (fig. 4 *A*), showed a more nearly normal position of the heart and expansion of the upper half of the left lung. By the third day the lung markings in the lower half were visible, and at the end of three weeks (fig. 4 *B*) the chest appeared normal. On the fifth day the baby showed a red throat and high fever, which gradually subsided, and at the end of two weeks he began to gain in weight. Both incisions healed without infection, and the child was discharged from the hospital, looking well and happy, exactly one month after admission. His weight was 11 pounds 2½ ounces (5,060 Gm.). Since that time almost three years has elapsed, and he has grown to be a strong, healthy lad (fig. 5), with no abnormality shown by either direct or roentgen examination.

In contradistinction to this experience we present our second case, representing the opposite extreme: difficulty in diagnosis, difficulty in preoperative preparation, great difficulty in the operative procedures and finally, fifteen months after the first of seven admissions to the hospital, death from bronchopneumonia.

Case 2.—J. B., a girl aged 19 days, was admitted to the Presbyterian Hospital, to the service of Dr. H. N. Sanford, on Feb. 29, 1936. She was born at home, the weight at birth being 7½ pounds (3,401 Gm.). The mother stated that two days after birth she had a violent choking attack and became cyanotic. Complementary feedings had been used. She had vomited frequently and had become cyanotic after each feeding. Examination on admission revealed an emaciated infant weighing 6 pounds 5 ounces (2,862 Gm.). She was slightly cyanotic. The blood count showed: hemoglobin, 80 per cent; red cells, 4,000,000; and white cells, 27,000, per cubic millimeter. No gross abnormalities could be made out, and the thoracic findings gave no clue to the presence of a diaphragmatic hernia. A flat roentgenogram of the chest, however, revealed a rounded air-containing pocket immediately behind the heart (fig. 6 *A*). When barium was given by mouth (March 5) it passed through a tortuous, dilated esophagus into a totally intrathoracic stomach, which when filled occupied the area just behind the heart and over the right dome of the diaphragm (fig. 6 *B*). The infant was given breast milk by gavage for a few days and then evaporated milk, water and sugar (eight feedings by bottle in twenty-four hours, with cod liver oil and orange juice). On March 21, when she left the hospital, she had gained, weighing 7 pounds 13 ounces (3,543 Gm.).

She was returned to the hospital about three weeks later (April 15), weighing 8 pounds 13 ounces (3,997 Gm.). She had done fairly well at home. There had been one attack of vomiting of coffee-like material and slight regurgitation after each feeding. The formula was changed to full strength lactic acid milk every

four hours, and she was discharged on April 21, weighing the same as on admission. On May 5 (about two weeks later) she was brought to the hospital for the third time. She had not done well at home; she vomited after almost every feeding and had lost 5 ounces (141.5 Gm.) in weight. Every effort was exerted during the next seven weeks to prepare her properly for operation, but great difficulties were encountered. However, by June 25 a gain of 1 pound 7 ounces (651 Gm.) had been accomplished; the blood count showed a hemoglobin content of 75 per cent; there were 4,900,000 red cells and 13,200 white cells per cubic millimeter, and after a small transfusion of blood from the father it was decided to proceed with the operation.

Operation was performed by Dr. Miller on June 25. The surgical approach in this case, of course, was different from that in the preceding case. Instead of an open defect in the diaphragm without any sac between the left upper quadrant of the abdomen and the left side of the chest, we were dealing with a paraesophageal hernia with a large sac occupying the mediastinum and a narrow neck near the midline. With the baby under ether anesthesia a left rectus incision

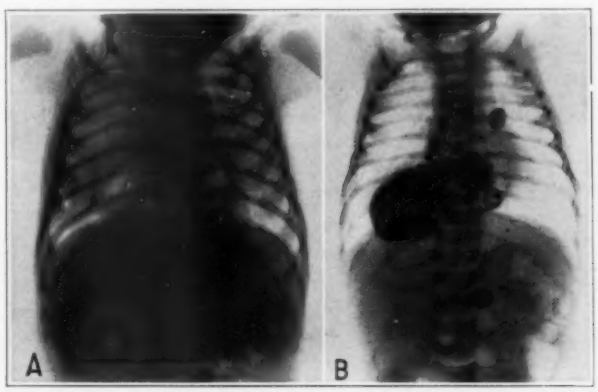

Fig. 6 (case 2).—*A,* roentgenogram of J. B., aged 19 days, with a paraesophageal hernia of the diaphragm. Note the round air-containing pocket immediately behind the heart. *B,* roentgenogram taken when the baby was 3 weeks old, showing the position of the stomach after the introduction of barium sulfate.

was made. The right lobe of the liver was retracted to the right of the aorta. In this opening lay the duodenum, and traction on it brought into view the greater curvature of the stomach. It was grasped with a Babcock forceps, and the entire stomach was gently and easily reduced to its normal position in the abdomen. The condition of the baby suddenly became very poor, and it was necessary rapidly to insert a running catgut suture to approximate the edges of the ring and effectively close the neck of the hernial sac. The postoperative progress was fair for several days, and the temperature ranged between 101 and 102 F. The child took small feedings by dropper fairly well, but at the end of a week the temperature was 104 F. and vomiting recurred. Fluoroscopic examination showed clouding of the lower half of the right lung field. On July 4, nine days after the operation, the condition was critical, and it was apparent from the rapid loss of weight, the obstructive symptoms and the vomiting of brown material that a recurrence of the herniation had occurred and that nothing short of an emergency operation could forestall a fatal result. Consequently, after this

diagnosis had been confirmed by introduction of a little barium sulfate through a tube, the baby was taken to the operating room, and under local anesthesia the abdomen was reopened, just to the right of the midline. The child's condition was very poor, and it was not easy to drag the swollen stomach down a second time through the neck of the sac, the margins of which were very edematous. During this maneuver several ounces of brown fluid escaped from the nose and mouth, and it was thought that the baby would die on the table. Very hurriedly a few interrupted stitches were inserted to narrow the neck of the sac, the liver was placed against this area and the stomach was anchored in position (fig. 7). The abdomen was quickly closed. The postoperative course was exceedingly stormy, and nothing but extreme effort on the part of the special nurses and the resident physicians of the pediatric and the surgical staff prevented death during

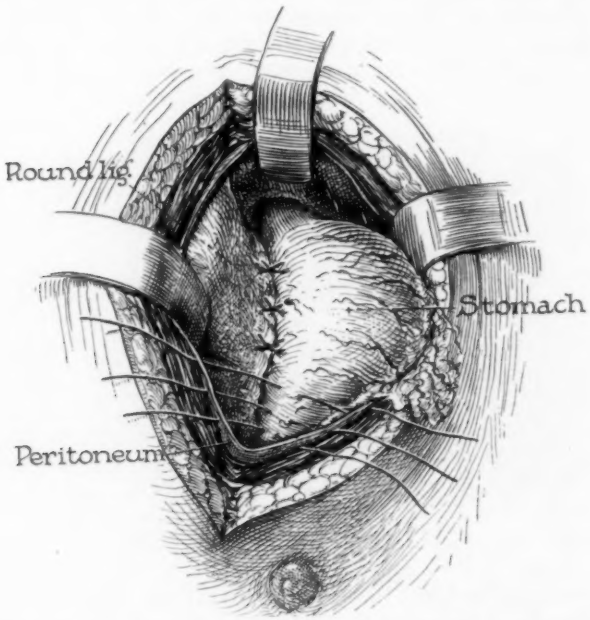

Fig. 7 (case 2).—Method of anchoring the stomach within the abdomen. Interrupted sutures of catgut were placed between the anterior wall of the stomach and the round ligament of the liver and also to the anterior parietal peritoneum.

the next few days. A Levine tube was constantly in place; the upright (almost sitting) position was maintained, and nourishment was introduced solely by vein and under the skin until a turn for the better was seen. When improvement had begun, small feedings of breast milk were given every two hours and 90 cc. of blood was given daily. The temperature remained constantly in the neighborhood of 105. The condition gradually improved for about a week, after which there was evidence of an infection of the upper part of the respiratory tract, succeeded by bronchopneumonia. For days the baby lay constantly under a steam tent; the signs of pneumonia gradually disappeared, and the temperature returned to normal. It goes without saying that we were all concerned over the question of the position of the stomach during this critical period. As soon, therefore, as the baby started to gain weight a small amount of barium sulfate was introduced and the position of the stomach within the abdomen verified (fig. 8). On September 25, eleven

weeks after the second operation, the child weighed 11 pounds 9 ounces (5,243 Gm.) and was discharged from the hospital.

Not long after this we began to consider reporting this case as one in which the operation was successful, but decided to wait until the baby had become entirely well and roentgen studies could be made to establish evidence of our success. This decision proved to make the difference between the report of a success and the report of a failure.

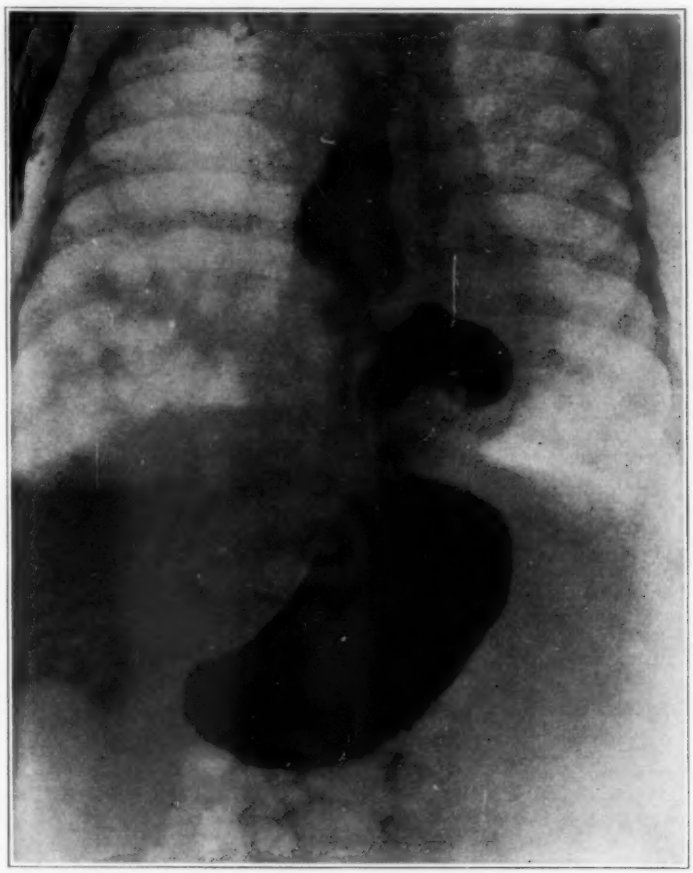

Fig. 8 (case 2).—Roentgenogram taken two and one-half months after the second operation. Note the dilated esophagus, the intra-abdominal position of the stomach and the air-containing loops of bowel occupying the hernial sac.

On November 16 the baby, now 9 months old and weighing 14 pounds 11 ounces (6,660 Gm.) was returned to the hospital for observation. She had done well at home until the last few days, when she had become feverish and had vomited a little. She was able to sit up alone, and she had two teeth. Her food was evaporated milk, water and sugar, two cereals, vegetables and one egg. The hemoglobin content of the blood was 80 per cent; the red cell count was 3,900,000 and the white cell count 7,000 per cubic millimeter. Severe bronchitis was present,

which accounted for the fever; this cleared up in a week, and she was discharged from the hospital on November 2, weighing 14 pounds 2 ounces (6,406 Gm.).

About five weeks later (December 30) she was again brought to the hospital (fifth admission) because during the past week she had vomited more or less after each feeding, her appetite was poor, there was a slight cough and she had lost 1 pound (453 Gm.) in weight. This time she remained in the hospital thirteen days, during which period the temperature returned to normal and the weight to 14 pounds 12 ounces (6,689 Gm.).

Three months later (April 5, 1937) she was again brought to the hospital, this time because of painful bowel movements and black stools. She was 14 months old and weighed 16 pounds 5 ounces (7,398 Gm.). After observation for twelve days she was discharged in fair condition, with only occasional vomiting and a

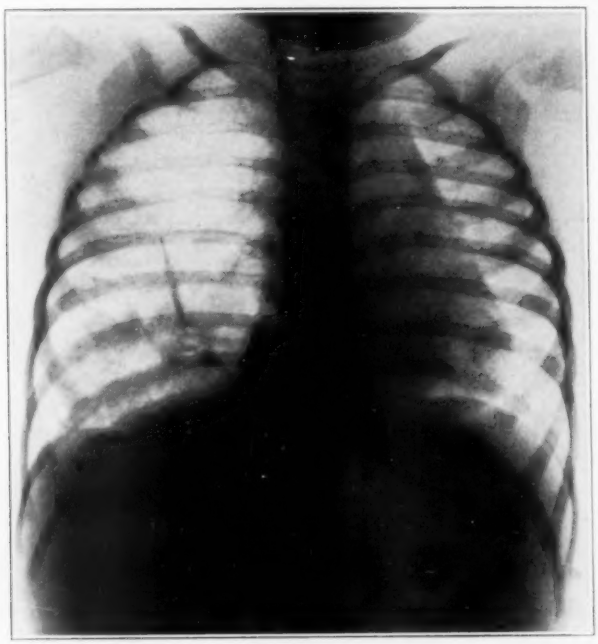

Fig. 9 (case 2).—Roentgenogram showing the faint outline of the hernial sac above the right side of the diaphragm.

constant weight. On May 22 she entered the hospital for the seventh and last time. Her age was 15 months and 12 days, and she weighed 17 pounds 6 ounces (7,881 Gm.) but she had not been doing well, in spite of the fact that her condition was fair. Her appetite had been fairly good and she ate regularly, but she had great difficulty with her bowels and great pain on passage of the stools. Roentgen examination (May 24) showed the heart deviated to the left; the lower half of the right lung field showed clearly the curved margin of the hernial sac (fig. 9) and within it several loops of bowel. Consultations resulted in a decision to operate again, with the object of reducing the contents of hernia, and, if possible, of closing the neck of the sac. On May 25 the abdomen was reopened through the old left rectus incision. The stomach was found to be in its normal position, entirely within the abdomen. It was lifted upward and retracted toward the right; this exposed the neck of the hernial sac, into which and from which led the trans-

verse colon (fig. 10). It had become so tightly wedged into the opening that it was reduced with considerable difficulty. It measured in length approximately 12 inches (33 cm.). The walls were edematous, and within the lumen could be felt some firm inspissated material. Closure of the neck of the sac was accurately made with a running suture of silk. Death occurred on the following day.

Autopsy.—There was paraesophageal hernia on the right, with an empty sac about the size of a large orange occupying the mediastinal space immediately behind and to the right of the heart. The stomach occupied a normal position; it was adherent anteriorly to the parietal peritoneum. There was no peritonitis. The neck of the hernial sac was completely closed except for an opening close

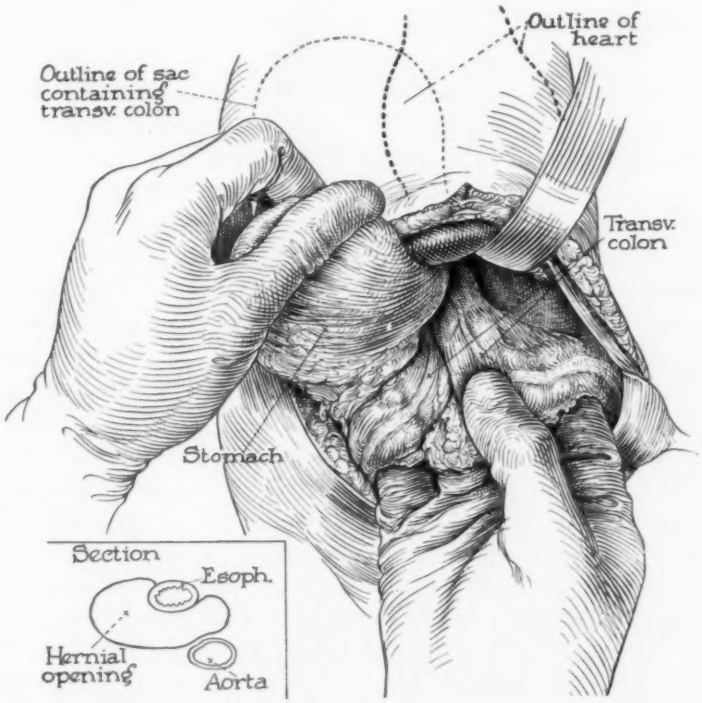

Fig. 10 (case 2).—Segment of the transverse colon in the hernial sac formerly occupied by the stomach.

to the spine, which admitted the tip of the finger. There was extensive bronchopneumonia of the left lung.

COMMENT

This second case illustrates the importance of making a snug closure of the neck of the hernial sac with nonabsorbable suture material; our failure to accomplish this at the first operation was responsible, we believe, for the trouble which followed later. It illustrates, also, the effectiveness of a method of anchoring the stomach in its normal position. If this also had been done at the first operation, the result might have been a success.

LESIONS OF THE SUPRASPINATUS TENDON AND ASSOCIATED STRUCTURES

INVESTIGATION OF COMPARABLE LESIONS IN THE HIP JOINT

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PHILADELPHIA

During a study of lesions in 150 shoulder joints, observations were made with regard to the abduction phase of shoulder motion which serve to corroborate the teachings of a small group of contemporary anatomists.

1. Abduction of the arm is a complex mechanism, involving the scapulohumeral, the acromioclavicular and the sternoclavicular joint, whereby the scapula moves along the chest wall, the humeral head glides within the glenoid cavity and the clavicle rotates as its lateral end moves dorsalward, the glenoid moving forward and upward. Toward the completion of abduction there is ipsilateral curvature of the dorsolumbar portion of the spine. In the bared specimen these joints demonstrate a range of motion far in excess of that normally required to elevate the arm.

2. Complete abduction can be obtained in the coronal plane only by external rotation of the humerus (Martin [1]) and in the sagittal plane by internal rotation of the humerus (Codman; [2] McGregor [3]). As the bared upper extremity of a human cadaver is elevated, one notes that the greater tuberosity glides posteriorly beneath the coracoacromial ligament and the acromion process where the interval between these structures and the humeral head is increased, carrying the humerus into external rotation; and as the arm is elevated in the sagittal plane, one observes that the lesser tuberosity abuts against the anterior part of the coracoacromial arch and glides internally, carrying the humerus into internal rotation. These movements are assisted by the gliding mechanism of the interposed bursae.

From the Daniel Baugh Institute of Anatomy, Jefferson Medical College, Prof. J. Parsons Schaeffer, Director.

1. Martin, C. P.: A Note on the Movements of the Shoulder-Joint, Brit. J. Surg. **20**:61, 1932.

2. Codman, E. A.: The Shoulder: Rupture of the Supraspinatus Tendon and Other Lesions In or About the Subacromial Bursa, Boston, The Author, 1934.

3. McGregor, L.: Rotation at the Shoulder: A Critical Inquiry, Brit. J. Surg. **24**:425, 1937.

3. By roentgenographic and fluoroscopic studies of the shoulder girdle in varying stages of abduction (fig. 1) it is observed that the scapula begins to move at the very onset of elevation of the arm from the side and that motion occurs in the scapulohumeral joint above the

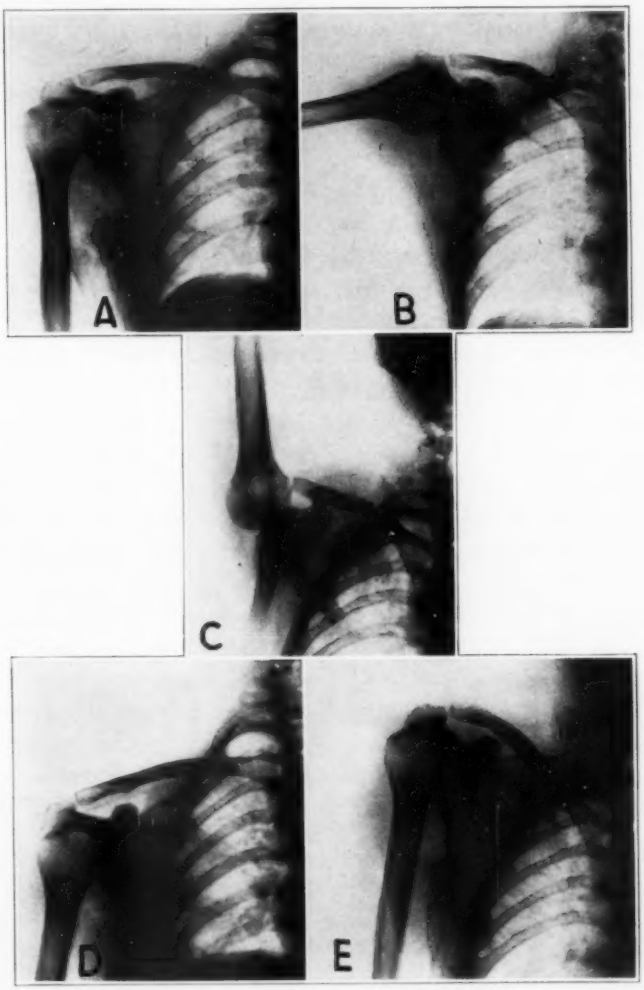

Fig. 1.—Normal shoulder girdle of a man aged 30. At *A* is shown the arm at rest at the side; at *B*, abduction to the horizontal plane; at *C*, complete abduction (pivotal position). Comparison of the position of the spine or vertebral border of the scapula in *A* and *B* indicates that the scapula rotates below the horizontal plane, while comparison of the amount of articular surface of the humerus that has left the glenoid cavity in *B* and *C* indicates motion of the scapulohumeral joint above this plane. (After Lockhart.)

At *D* is shown the maximum depression and at *E* the maximum elevation of the shoulder girdle without scapulohumeral motion, indicating the reserve range of motion possible in the sternoclavicular and acromioclavicular joints, which exceeds that required in complete abduction normally (*A* to *C*).

horizontal plane. This confirms the observations of Cathcart [4] and Lockhart.[5]

4. To analyze the function of the individual muscular components involved in abduction, cases of isolated paralysis of the deltoid, the trapezius, the serratus anterior and the supraspinatus muscle and recent tears of the last-named muscle were analyzed from the literature and from my own clinical material.

The importance of the action of the supraspinatus muscle in furnishing a fulcrum for the humeral head in the glenoid cavity for the action of the deltoid muscle has been stressed by Stevens [6] and by Codman. Early, in its absence, abduction cannot be initiated. The fact that abduction is restored in cases of long-standing involvement despite the persistence of demonstrable tears of the supraspinatus muscle (Codman) indicates that one or more of the other short rotators may effectively assume the function of the supraspinatus muscle.

In the presence of localized paralysis of the deltoid muscle due to injury of the circumflex nerve (Smith and Christensen [7]) the arm cannot be abducted at the shoulder joint even with the supraspinatus muscle intact. In cases of involvement of long duration this deficiency is partially overcome by substitutionary action, especially of the long heads of the biceps and the triceps muscle. Abduction by action of the supraspinatus muscle alone, as reported by Duchenne [8] and Codman, is unusual.

The trapezius and the serratus anterior muscle become active immediately as the arm leaves the side. In the presence of isolated paralysis of the former muscle (Lockhart,[5] Beevor [9]) there are slight "winging" and weakness in the early stage of abduction, which disappear as the mechanical efficiency of the serratus anterior muscle increases. In the presence of isolated paralysis of the serratus anterior muscle, "winging" is marked, and abduction is limited below the horizontal plane. The

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5. Lockhart, R. D.: Movements of the Normal Shoulder Joint and of a Case with Trapezius Paralysis Studied by Radiogram and Experiment in the Living, J. Anat. **64**:288, 1930.

6. Stevens, J. H.: The Action of the Short Rotators on the Normal Abduction of the Arm with a Consideration of Their Action in Some Cases of Subacromial Bursitis and Allied Conditions, Am. J. M. Sc. **138**:870, 1909.

7. Smith, J. F., and Christensen, H. H.: Deltoid Paralysis Following Shoulder Injuries, Surg., Gynec. & Obst. **41**:451, 1925.

8. Duchenne, G. B.: Physiologie des mouvements, Paris, J. B. Baillière et fils, 1867.

9. Beevor, C. E.: The Croonian Lectures on the Central Nervous System, Brit. M. J. **1**:1357, 1903.

protagonistic action of the long head of the triceps muscle to abduction has been stressed elsewhere (Horwitz and Tocantins [10]).

5. The "neutral position" is necessary in the treatment of injuries to the shoulder to place the shoulder muscles at rest, to prevent contractures and to place the arm in a functional position if it stiffens. This requires that the arm be (1) in the horizontal plane, (2) in the plane of the scapula, i. e., 30 degrees anterior to the coronal plane of the body, to avoid torsion of the inferior capsule (Johnston [11]) and tension of the pectoralis major muscle (Böhler [12]), and (3) rotated to a position 45 degrees less than that of complete external rotation, since the arc of rotation of the arm in the horizontal plane is 90 degrees (Codman). Since abduction has been shown to continue in the scapulohumeral joint from 20 to 30 degrees above the horizontal plane, it is logical to recommend this extent of abduction (120 degrees), suggested by Mayer [13] after surgical correction of rupture of the supraspinatus tendon, to insure approximation of the tendinous ends.

PATHOLOGIC FINDINGS

As acknowledged by Codman,[14] Smith [15] in 1834 reported 7 instances of destruction of the upper part of the shoulder capsule in 40 anatomic dissections, 5 of these involving the musculotendinous cuff. Akerson, cited by Codman,[2] found 64 tears of the supraspinatus tendon in 200 shoulder joints (32 per cent) and associated tears in other portions of the musculotendinous cuff in 30 instances. The injury was most frequent in males (2:1) and was bilateral in 14 of the first 100 specimens. Keyes [16] noted 24 tears of the supraspinatus tendon in 192 shoulder joints (17 per cent). The patients were equally divided as to sex; the youngest was 45 years old and the average age was 53. Skinner [17]

10. Horwitz, M. T., and Tocantins, L. M.: Isolated Paralysis of the Serratus Anterior (Magnus) Muscle, J. Bone & Joint Surg. **20**:720, 1938.

11. Johnston, T. B.: The Movements of the Shoulder Joint: A Plea for the Use of the "Plane of the Scapula" as the Plane of Reference for Movements Occurring at the Humeroscapular Joint, Brit. J. Surg. **25**:252, 1937.

12. Böhler, L.: The Treatment of Fractures, ed. 4, translated by E. W. H. Groves, Baltimore, William Wood & Company, 1935.

13. Mayer, L.: Rupture of the Supraspinatus Tendon, J. Bone & Joint Surg. **19**:640, 1937.

14. Codman, E. A.: Rupture of the Supraspinatus—1834 to 1934, J. Bone & Joint Surg. **19**:643, 1937.

15. Smith, J. S.: Pathological Appearance of Seven Cases of Injury of the Shoulder Joint, with Remarks, Am. J. M. Sc. **16**:210, 1835; London M. Gaz. **14**: 280, 1834.

16. Keyes, E. L.: Anatomical Observations on Senile Changes in the Shoulder, J. Bone & Joint Surg. **17**:953, 1935.

17. Skinner, H. A.: Anatomical Considerations Relative to Rupture of the Supraspinatus Tendon, J. Bone & Joint Surg. **19**:137, 1937.

observed 6 such tears in 100 shoulder joints, and Fowler [18] in a series of 340 specimens noted 1 complete tear of the supraspinatus tendon in every 28 and 1 incomplete tear in every 6 shoulder joints.

While the clinical features of tear of the supraspinatus tendon have been stressed by Codman, this careful observer up to 1934 had never observed a tear less than three weeks after injury and admitted that, although this clinical diagnosis had been corroborated at the operating table in 29 cases, in 16 others no such lesion could be demonstrated.[18a] Wilson [19] in 1931 reported the demonstration of tears of the supraspinatus tendon at the operating table in 10 instances. These defects, varying in size from 1 to 2½ inches (2.5 to 6.3 cm.) in diameter, occurred in patients in the fourth decade of life, except in 1 case, in which the patient was 35. Recent tears have been demonstrated by Ferguson [20] four days after injury, by Mayer [13] forty-eight hours after injury and by Davis and Sullivan [21] in 5 cases within seventeen days after the initial trauma. In 12 cases, reported by Outland and Shepherd,[22] 1 lesion in a patient aged 32 and 2 in patients aged 42 followed dislocation of the shoulder The ages of the remaining patients ranged above 50.

PERIARTICULAR AND ARTICULAR CHANGES IN THE SHOULDER JOINT

Of the 75 cadavers (150 shoulder joints) utilized in this study, 71 were male and 4 female. The average age at death was 55, the ages varying from 35 to 82.

1. *Changes in Bursae (Subacromial; Subdeltoid; Subcoracoid).*—In 30 specimens variable changes were noted, with thickening of the walls, villous formation and partial or complete obliteration of the bursal cavity. In 10 specimens the cavity of the bursa communicated with the shoulder joint owing to a complete defect in the bursal floor, i. e., tear of the supraspinatus tendon. In 3 specimens, in each of which

18. Fowler, E. B.: Stiff, Painful Shoulders, Exclusive of Tuberculosis and Other Infections, J. A. M. A. **101**:2106 (Dec. 30) 1933.

18a. In a recent contribution, Codman reported a fresh rupture of the supraspinatus tendon, diagnosed forty-eight hours after, and visualized seven days after, injury (Codman, E. A.: Rupture of the Supraspinatus, Am. J. Surg. **42**:603 [Dec.] 1938).

19. Wilson, P. D.: Complete Rupture of the Supraspinatus Tendon, J. A. M. A. **96**:433 (Feb. 7) 1931.

20. Ferguson, L. K.: Suture of Ruptured Supraspinatus Tendon Four Days After Injury, Am. J. Surg. **29**:294, 1935.

21. Davis, J. W., and Sullivan, J. E.: Rupture of the Supraspinatus Tendon, Ann. Surg. **106**:1059, 1937.

22. Outland, T. A., and Shepherd, W. F.: Tears of the Supraspinatus Tendon, Ann. Surg. **107**:116, 1938.

the subcoracoid bursa was separated from the main subacromial (subdeltoid) bursa by a complete partition, the former showed degenerative changes, a large calculus filling it in 1 instance, while the subacromial bursa appeared normal. In no other instance were calcium deposits found within or about the bursae.

2. *Changes in the Musculotendinous Cuff (Supraspinatus, Infraspinatus, Teres Minor, and Subscapularis Tendons).*—There were 10 complete tears of the supraspinatus tendon (6.67 per cent), the cavity of the subacromial bursa communicating directly with the shoulder joint. From the standpoint of statistical evaluation it is noteworthy that only

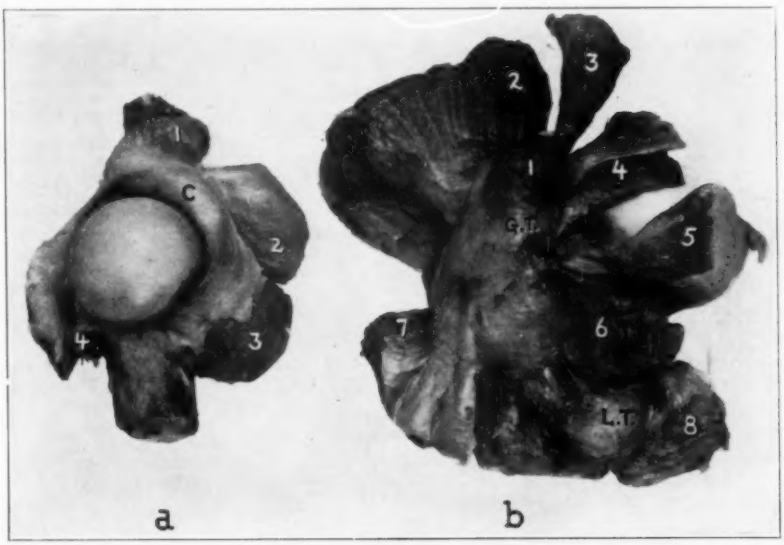

Fig. 2.—At *a* is shown the musculotendinous cuff merging intimately with the joint capsule (*C*) about the anatomic neck of the right humerus, as viewed from the articular side (*1*, supraspinatus muscle; *2*, infraspinatus muscle; *3*, teres minor muscle; *4*, subscapularis muscle). At *b* is shown the musculotendinous cuff (*2* to *6* inclusive) encircling the neck of the left femur, as viewed posteriorly. Bursae cover the great trochanter (*G.T.*) and the lesser trochanter (*L.T.*). Point *1* indicates the gluteus medius muscle; point *2*, the gluteus minimus muscle; point *3*, the piriformis muscle; point *4*, the superior gemellus, the obturator internus and the inferior gemellus muscle; point *5*, obturator externus muscle; point *6*, the quadratus femoris muscle; point *7*, the vastus lateralis muscle; and point *8*, the psoas major muscle.

1 such tear was observed in the first 100 shoulder joints studied, the other 9 being uncovered in the next 50 specimens. These tears were bilateral in 3 and unilateral in 4 cadavers. Six involved the right side

and 4 the left. All occurred in males, the youngest of whom was 50.[22a] The average age for the series of 10 (figs. 3 and 4) was 58.

In no instance was there gross evidence of calcific deposits in or about the supraspinatus tendon, although roentgenographic and microscopic studies might have revealed small deposits (Keyes[16]). In 49 specimens the upper (cephalic) portion of the musculotendinous cuff showed variable amounts of thinning, measuring in some instances only 1 to 2 mm. In 30 cases the superficial surface of the supraspinatus ten-

Tears of the Supraspinatus Tendon

	Extent of Lesion	Shape	Changes in Other Portions of Musculotendinous Cuff	Changes in Bicipital Tendon	Changes in Bone
1	Complete in thickness and entire width of tendon	Circular	Fibrillation and fraying of subscapularis and infraspinatus muscle	Flattening and fraying	Hypertrophic marginal articular changes; recession of great tubercle
2	Complete in thickness and entire width of tendon	Oval, in long axis of tendon	Tear of subscapularis and thinning of infraspinatus muscle	Complete tear; proximal portion absent and distal portion attached to lesser tubercle	Hypertrophic changes about tubercles and margins of bicipital groove
3	Complete in thickness but involving only partial width of tendon	Oval	Fraying and incomplete tears ("rim rents") of deep surface of subscapularis muscle	Proximal portion attached to articular surface; distal portion attached to lesser tubercle	Hypertrophic changes about tubercles and margins of bicipital groove
4, 5, 6, 7 and 8	Complete in thickness but involving width only partially	Oval	Fraying and incomplete tears of deep surface of subscapularis muscle	Flattening, fraying and thinning	Proliferative changes less marked
9	Complete in thickness; 6.5 mm. wide	Triangular	Slight fraying of subscapularis tendon	Slight fraying	Slight
10	Complete in thickness; 5 mm. wide	Semicircular	Large gap between supraspinatus tendon and subscapularis tendon, which were frayed and thinned	Flattening and fraying	Moderate proliferative and recessive changes

don was frayed and fibrillated, with separation of the tendon fibers to form bands or "straps" (Codman). In many of these cases fissures ("rim rents") of the deep, or articular, surface of the tendon were noted. In these cases involvement of the subscapularis tendon was almost as advanced, while changes in the infraspinatus tendon were less marked, and in the teres minor tendon they were usually absent (figs. 3 and 4).

22a. In a study of 100 additional human shoulder joints, 7 complete defects of the supraspinatus tendon were disclosed, all in males, occurring bilaterally in 2 cadavers and unilaterally (right) in 3. The total incidence of tears of the supraspinatus tendon is 17 instances in 250 shoulder joints, or 6.8 per cent.

3. *Changes in the Biceps Tendon and Bicipital Groove.*—In 75 specimens the portion of the long bicipital tendon within the groove was constricted, although it was otherwise normal. In 30 instances varying stages of flattening, thinning, fraying, fibrillation and tearing were evident, such changes being usually associated with bony changes about the tubercles and the bicipital groove (fig. 5). There were 4 complete tears, and in each the proximal end of the distal portion had become

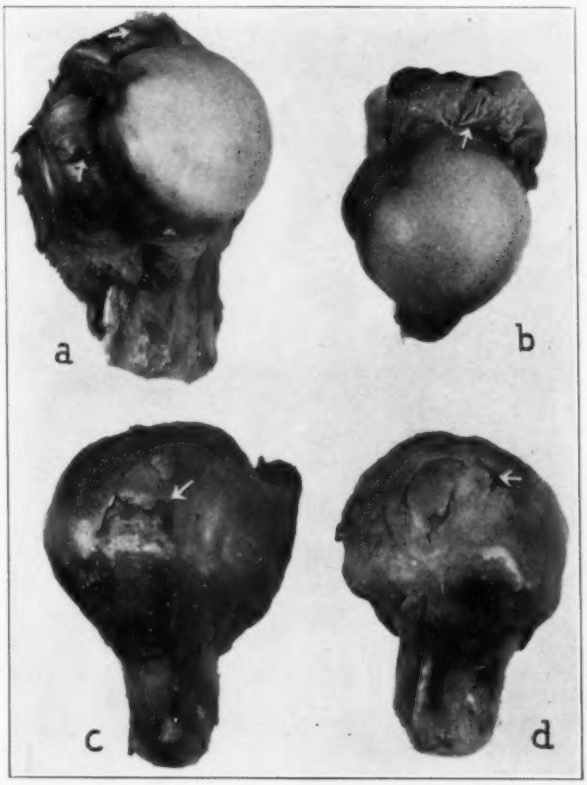

Fig. 3.—At *a* is shown fraying, fibrillation and thinning of the deep surface of the tendons of the supraspinatus, infraspinatus and subscapularis muscles; at *b*, longitudinal fissures ("rim rents") of the deep surface of the reflected supraspinatus tendon; at *c*, a triangular defect ¼ inch (6.5 mm.) wide, near the insertion of the supraspinatus tendon, the greater tubercle being exposed and showing early recessive changes; at *d*, a complete defect in the supraspinatus tendon, ½ by 1 inch (25 by 12.5 mm.) with the exposed biceps tendon flattened and frayed. The adjacent portion of the cuff is thinned and its deep surface frayed and fibrillated.

dislocated medially out of the groove and attached to the region of the lesser tubercle. In 1 of these specimens the proximal portion had completely disappeared; in 2 a small stub remained attached to the supra-

glenoid tubercle, while in the fourth the proximal portion had become attached to the articular surface of the humerus like a ligamentum teres (fig. 5). In one instance the tendon was firmly bound down within its groove by adhesions.

4. *Bony Changes.*—These seemed proportional to the amount of alteration in the soft tissues. Proliferative changes (fig. 6) involved especially the greater and lesser tubercles and the margins of the bicipi-

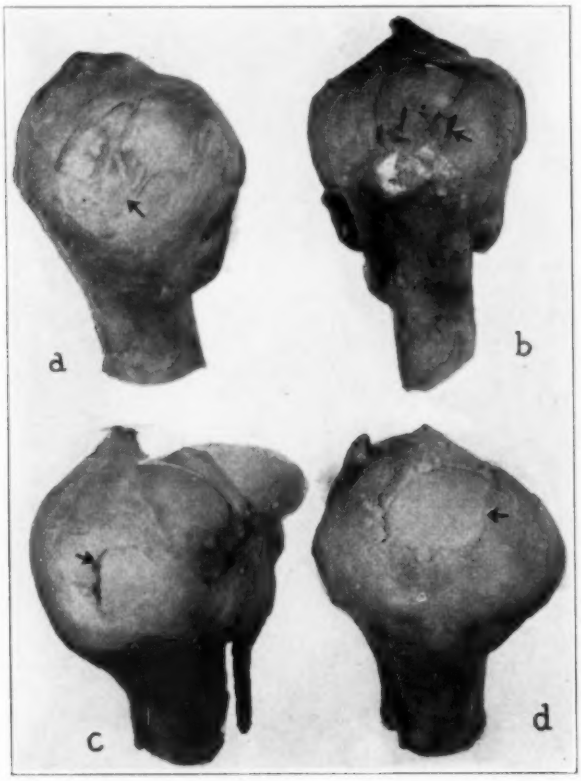

Fig. 4.—At *a* is shown complete defect in the supraspinatus tendon, 1 inch (25 mm.) in its widest diameter, with fraying and the formation of bands or "straps." The greater tubercle is exposed, with hypertrophic and recessive changes. At *b* is shown a complete defect measuring 1 by ¼ inch (25 by 6.5 mm.), with formation of "straps." The adjacent cuff is thinned and frayed on its deep surface. Note the recessive changes in the exposed greater tubercle. At *c* is shown a large gap existing between the remains of the supraspinatus tendon and the subscapularis tendon. A semicircular, complete defect is present in the supraspinatus tendon close to its insertion. At *d* is shown the largest defect uncovered in the supraspinatus tendon. The defect was circular and measured 1 and ¼ inches (31 mm.) in diameter. The remainder of the cuff was thinned and fibrillated. The biceps tendon was flattened and frayed.

tal groove, occasionally encasing the long biceps tendon. When the latter tendon had been dislocated or torn the bicipital groove had become shallow or obliterated. In instances in which, owing to a large defect in the cephalic portion of the musculotendinous cuff, the greater tubercle was exposed there was evidence of bony recession and atrophy. Similar changes on the under surface of the acromion process evidenced the effects of long-continued friction between these bony surfaces. In many of the same cases the articular cartilage showed degenerative changes, with marginal lipping most marked at the superior and anterior borders. Occasionally the cartilage was denuded in areas, with

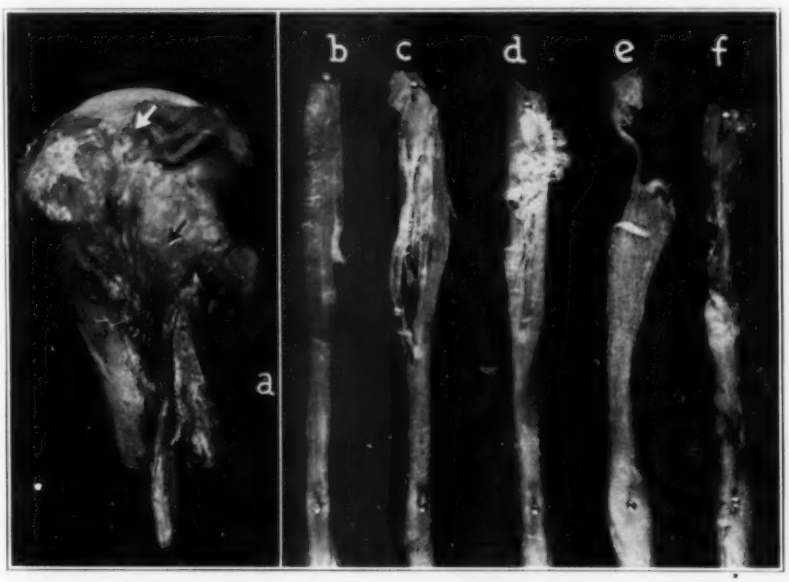

Fig. 5.—At *a* is shown the long bicipital tendon completely severed, the proximal segment having reattached itself to the articular surface and the distal segment to the lesser tubercle. Note the recession of the greater tubercle, marginal proliferation and obliteration of the bicipital groove. The tendons lettered from *b* to *f* are long bicipital tendons showing varying stages of flattening, fibrillation, fraying and tearing.

exposure of the underlying bone, which was often eburnated and glistening owing to constant friction.

PERIARTICULAR AND ARTICULAR CHANGES IN THE HIP JOINT

The hip joint in this same series of cadavers was investigated, with attention to changes in its numerous bursae, in the muscles and tendons and in the joint itself. While the hip joint, like the shoulder joint, is an enarthrodial joint, it depends for its stability, unlike the latter, on its

bony architecture and not on its soft tissue structures. It is therefore not remarkable that comparable lesions were infrequently noted.

The great trochcanteric bursa, frequently observed to be partitioned by many synovial folds, was occasionally completely divided into an upper and a lower bursa. In 15 cases its walls were thickened and its inner lining frayed and at times partially or completely adherent. The iliopectineal bursa communicated with the joint cavity in 10 per cent of cases, often bilaterally. In 10 instances this bursa was partially or completely obliterated. No changes were observed in the other bursae

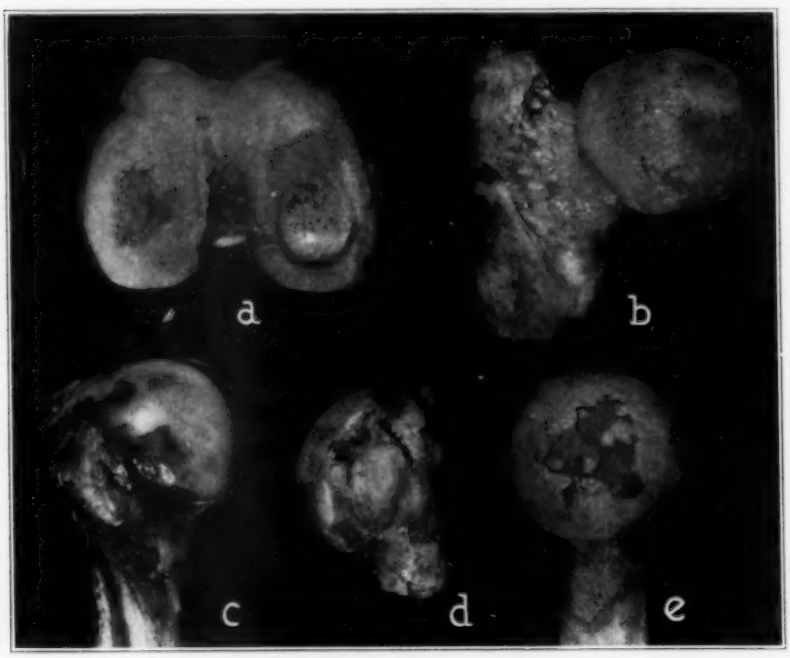

Fig. 6.—Degenerative lesions of the cartilage, with denudation of the underlying bone in areas and secondary eburnation. Hypertrophic changes are present along the margins of the articular surfaces. At *a* is shown the distal articular surface of the femur; at *b*, the head and neck of the femur; at *c*, *d* and *e*, heads and necks of humeri.

of the hip joint. The relation of infections of the bursa of the great trochanter to the fascial compartments of the thigh has been stressed by Milgram,[23] and the symptom complex of iliopectineal bursitis has been reviewed recently by Finder.[24]

23. Milgram, J. E.: Surgery of Suppuration in the Fascial Spaces of the Thigh, J. A. M. A. **98**:117 (Jan. 9) 1932.

24. Finder, J. G.: Iliopectineal Bursitis, Arch. Surg. **36**:519 (March) 1938.

No gross changes were noted in the tendons of the short rotators and abductors which insert about the base of the neck of the femur and merge with the capsule of the hip joint in a manner similar to that of the musculotendinous cuff about the head of the humerus (fig. 2). In only 1 instance, in which there was a comminuted fracture of the

Gluteus medius
Thickened walls of greater trochanteric bursa.
Calcific deposits perforating floor of bursa
Gluteus maximus

Fig. 7.—Artist's representation of calcific deposits embedded in the floor of a thick-walled great trochanteric bursa in a case of ununited fracture of the base of the neck of the femur.

base of the femoral neck, were advanced changes noted in the floor of the bursa of the great trochanter, two large calcific deposits lying deeply embedded within the fibrillated fibers of the vastus lateralis muscle (fig. 7). The roentgenographic evidence of calcific deposits about the greater trochanter in 30 out of 550 (5.4 per cent) patients aged from

15 to 69, reported by Goldenberg and Leventhal,[25] indicates that slight changes, not grossly evident, might have been revealed by roentgenographic and microscopic studies.

COMMENT

Codman [2] has admitted that since in most of his cases tear of the supraspinatus tendon occurred in aged persons and many of the tears were bilateral, some form of necrosis may have been largely responsible for the lesions and also for their failure to repair. He has been tempted to compromise on the theory that many causes or combinations of causes —age, constitutional factors, calcific deposits within the supraspinatus tendon, or overuse—might result in the same lesion, but he stated that he was convinced that trauma produces the actual rupture in most instances and that the defect should be surgically repaired.

Wilson [19] noted in his cases that, in addition to the actual rupture, degenerative lesions were present in the unruptured portions of the musculotendinous cuff. He stated:

> One cannot avoid the opinion that there are signs of gradual deterioration of the tendon from the excessive use and advancing age with perhaps defective circulation in the background. These changes probably precede and pave the way for rupture of the tendon and this view explains why in many instances rupture finally occurs under conditions that approximate normal use.

There is much evidence to support Meyer's hypothesis of attrition,[26] namely, that in addition to trauma and long-continued friction there is a failure of bodily reparative processes to function adequately. This author has stressed concomitant degenerative lesions in other tissues of the shoulder joint, attritional lesions in other joints of the body, the oval or circular rather than transverse shape of the tendinous defect and the absence of atrophy of the muscle bellies of the completely torn tendons (supraspinatus and long bicipital). He has noted that according to Cronkite and others [27] a supraspinatus tendon ¾ inch (1.9 cm.) wide and 2 mm. thick can bear a pull of 700 pounds and one 3 mm. thick a pull of 1,000 pounds; rupture of a sound supraspinatus tendon which is more than 3 mm. thick is therefore highly improbable. McMaster [28] has demonstrated experimentally that when a sound muscle is subjected to

25. Goldenberg, R. R., and Leventhal, G. S.: Supratrochanteric Calcification, J. Bone & Joint Surg. **18**:205, 1936.

26. Meyer, A. W.: Chronic Functional Lesions of the Shoulder, Arch. Surg. **35**:646 (Oct.) 1937.

27. Cronkite, A. E.: The Tensile Strength of Human Tendons, Anat. Rec. **64**: 173, 1936.

28. McMaster, P. E.: Tendon and Muscle Ruptures: Clinical and Experimental Studies on the Causes and Location of Subcutaneous Ruptures, J. Bone & Joint Surg. **15**:705, 1933.

strong traction tears will occur at its origin and insertion and in the muscle belly but not in the tendon itself.

The relation of the anatomic changes produced by degenerative arthritis to advancing age, wear and tear, stress, trauma, occupation, and static deformities has been stressed by Keefer and his co-workers,[29] Meyer [30] and Keyes [31] for human joints, by Bennett and Bauer [32] for bovine joints and by Glauning,[33] Callender and Kelser [34] and others for the articulations of horses.

CONCLUSION

From this evidence I am convinced that the symptom complex of rupture of the supraspinatus tendon represents the effects of trauma, often minimal, on tissues which are the site of degenerative lesions incidental to advancing age, defective circulation, excessive use and attritional changes. The fact that such a lesion is demonstrated at autopsy and in the dissecting laboratory in cases in which there is no history of injury and its high incidence in adult cadavers, especially those of persons advanced in years, indicate that trauma serves merely to hasten the progress of pathologic events already taking place. The wisdom of subjecting a patient with such a condition to surgical procedures is therefore to be questioned.

Defects in the tendons of a patient prior to the fourth decade of life are secondary in most instances to inflammatory processes and calcific deposits, occur less frequently and require relatively severe trauma to further the disruption of the tendon. Surgical repair seems justified in this small group of cases to correct not only the secondary, but also the primary, defect.

Twentieth and Chestnut Streets.

29. Keefer, C. S.; Parker, F., Jr.; Myers, W. K., and Irwin, R. L.: Relationship Between Anatomic Changes in the Knee Joint with Advancing Age and Degenerative Arthritis, Arch. Int. Med. **53**:325 (March) 1934.

30. Meyer, A. W.: Use Destruction in the Human Body, California & West. Med. **47**:375, 1937.

31. Keyes, E. L.: Erosions of the Articular Surfaces of the Knee Joint, J. Bone & Joint Surg. **15**:369, 1933.

32. Bennett, G. A., and Bauer, W.: A Systematic Study of the Degeneration of Articular Cartilage in Bovine Joints, Am. J. Path. **7**:399, 1931.

33. Glauning, W.: Altersveränderungen im Kniegelenk des Pferds, Inaug. Dissert., Regensburg, Josef Habbel, 1936; cited by Meyer.[26]

34. Callender, G. R., and Kelser, R. A.: Degenerative Arthritis: A Comparison of the Pathological Changes in Man and Equines, Am. J. Path. **14**:253, 1938.

RESECTION OF THE CARCINOMATOUS RECTOSIGMOID JUNCTURE

WITH REESTABLISHMENT OF INTESTINAL CONTINUITY: PRELIMINARY REPORT

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SAN FRANCISCO

The rectosigmoid, or retrosigmoid juncture, is that part of the bowel opposite the reflection of the peritoneum in the lowermost portion of the pelvic cavity. Clinically the terminal inch (2.5 cm.) of the sigmoid flexure of the colon and the uppermost inch of the rectum are considered as composing it. Next to the stomach the rectum is the most common site of malignant disease of the gastrointestinal tract. It is generally accepted that rectal carcinomas make up about 4 per cent of all carcinomas and that about 80 per cent of intestinal carcinomas appear in the rectum. Rankin and his associates [1] stated:

> We believe that most carcinomas of the rectum are at the rectosigmoid juncture, that the next point of frequency is in the ampulla of the rectum, and that the site of least frequency is the anal canal and the lower five or six cm. of the rectum.

One is impressed with the high incidence of carcinoma involving this portion of the bowel. It follows that a surgeon who makes a permanent abdominal colostomy opening with removal of the lower part of the bowel for carcinoma of the lower portion of the sigmoid flexure and the rectum does so in most instances for carcinoma of the rectosigmoid juncture. If a satisfactory operation could be devised for removal of the carcinomatous rectosigmoid and reestablishment of the continuity of the bowel, leaving the patient with a normal anus, it would be a great boon to that unfortunate group who heretofore have been left with an abdominal anus after the removal of the rectosigmoid for malignant disease.

I have developed and used such an operation and believe others can apply it successfully in selected cases of carcinoma of the rectosigmoid. The technic involved is not new but is a combination of well known procedures, the rectosigmoid being resected in a one stage abdominosacral operation and continuity of the sigmoid flexure and the rectum being reestablished (by means of the Mikulicz technic)

1. Rankin, F. W.; Bargen, J. A., and Buie, L. A.: The Colon, Rectum and Anus, Philadelphia, W. B. Saunders Company, 1932.

immediately below the sacrum. Crushing clamps are left on the proximal and distal ends of the bowel, to be removed in about forty-eight hours, after which, a few days later, right angle clamps are applied to cut through the septum.

OPERATION

The abdomen is opened by a paramedian incision on the right, extending from the symphysis pubis to about 1 inch (2.5 cm.) above the umbilicus. A self-retaining retractor is adjusted, and the abdomen is explored to determine operability. All of the bowel except the descend-

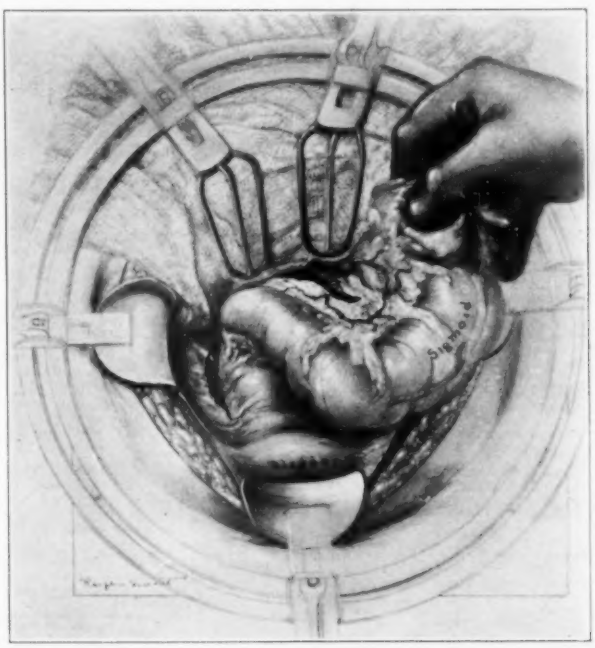

Fig. 1.—Abdomen held open by a circular retractor, the viscera being held in the upper part of the abdomen by self-retaining visceral retraction. An oval rent has been made in the mesosigmoid, extending down toward the pelvis. The superior hemorrhoidal artery has been ligated above the "critical point." The mesial and lateral peritoneal incisions are shown.

ing colon is placed in the upper part of the abdomen and held there by packs. I have devised a special circular retractor (fig. 1) which permits self-retaining visceral retraction as well as parietal retraction. The lower portion of the sigmoid flexure is pulled up, the mesosigmoid being spread into the shape of a fan. The superior hemorrhoidal and the sigmoid artery are identified. The peritoneum of the mesosigmoid is opened mesially about opposite the bifurcation of the aorta. The

superior hemorrhoidal artery is doubly ligated and is severed between ligatures proximal to its branching to form a part of the marginal artery (fig. 1). The opening in the mesosigmoid is continued through to the lateral side. By enlargement of this rent downward the pelvic portion of the colon is mobilized, but the blood supply is not materially affected, because the continuity of the marginal artery is not interrupted. A wedge-shaped piece of the node-bearing mesosigmoid is removed with the distal portion of the sigmoid flexure. An incision is made in the peritoneum of the mesentery on the mesial side of the pelvic portion of the colon and is carried down to the bladder. A similar incision is

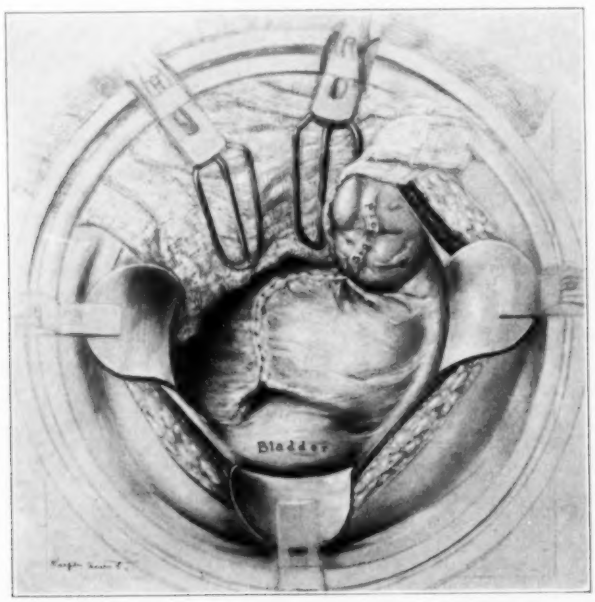

Fig. 2.—Abdomen held open by a retractor. The pelvic floor has been reestablished.

made on the left side of the bowel and is carried down to the reflection of the peritoneum at the base of the pelvic cavity. The left ureter comes into view. The lower ends of the incisions are connected by a transverse incision through the peritoneum. The edges of the peritoneum so incised are dissected free, and the peritoneal bands holding the bowel to the bladder are severed with scissors. The bowel is freed anteriorly down as far as possible into the pelvis. The distal portion of the sigmoid flexure is now lifted up, and a hand is inserted posterior to it, freeing it from the sacrum down to the coccyx. The terminal

portion of the sigmoid flexure and the rectosigmoid are now pushed down into the pelvis, and a new, high pelvic floor (fig. 2) is established by approximation of the lateral peritoneal flaps and suturing of their upper ends across the anterior portion of the sigmoid flexure to its anterior peritoneal covering. Thus the peritoneal cavity is entirely closed. The descent of the distal portion of the sigmoid flexure is made possible by the severance of the superior hemorrhoidal artery and the rent made in the mesosigmoid. The abdomen is closed in the usual way, and the patient is placed on his right side. The sacrum and the perineal region are prepared; the anus is closed with a purse

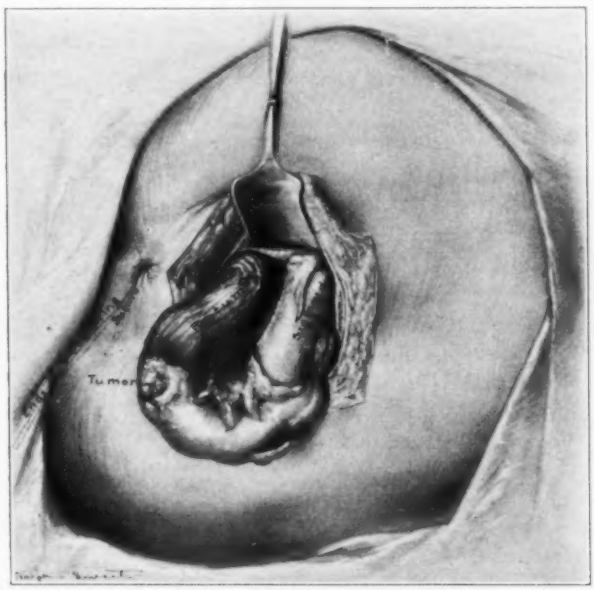

Fig. 3.—Patient in the right lateral position. (The left lateral position may be used.) The purse string suture on the anus and the T-shaped sacral incision can be seen. The rectosigmoid has been pulled through the incision. The limbs of the bowel have been sutured as with the Mikulicz procedure. The coccyx has been removed.

string suture, and an incision is made in the midsacral line from a point 1 inch above the anus to the sacrococcygeal articulation. At this point a transverse incision is made, forming a T-shaped incision. These incisions are carried deeper, and the coccyx is disarticulated. The posterior aspect of the bowel is exposed. The fascia propria is divided opposite the sacrococcygeal articulation, and the bowel is dissected free from the sacrum. The middle sacral artery may require ligatures. The rectosigmoid is dissected free from its lateral attachments and

anteriorly until a finger can be inserted around the bowel below the tumor. An ordinary hernia tape is inserted around the bowel and used for traction. The rectosigmoid is mobilized up to the pelvic floor. The rent in the mesosigmoid now comes into view, and the peritoneal covering of the distal portion of the sigmoid flexure is seen. The loose perirectosigmoidal tissues and node-bearing glands are dissected out. The rectosigmoid is now pulled out through the sacral incision (fig. 3); several nonpenetrating sutures are used to unite the serosae of the limbs of the intestinal loop on either side, and two crushing clamps are placed on the bowel at a safe distance from the growth, above and

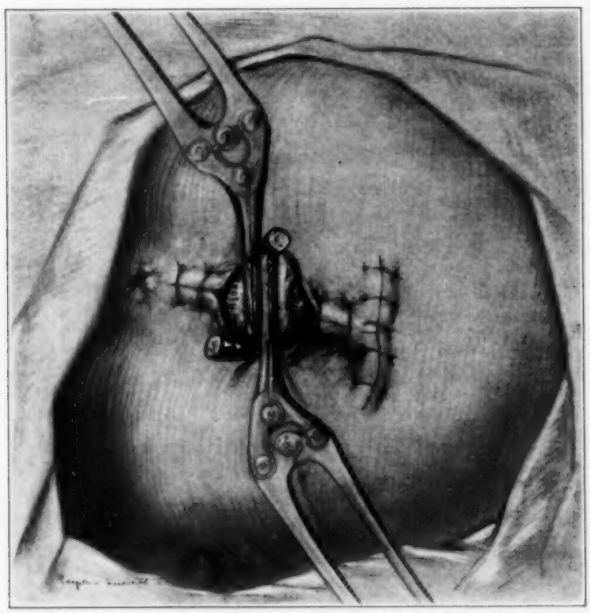

Fig. 4.—Crushing clamps in place. A segment of bowel has been removed. The T-shaped incision has been sutured. The purse string suture has been removed from the anus. Small cigaret drains have been placed on either side of the bowel. (Straight Kocher forceps may be used instead of heavy crushing clamps, since they are more easily taped to the buttocks. Instead of using forceps one may tie the ends of bowel with braided silk ligatures.)

below the rectosigmoid. The bowel is severed with a cautery both distally and proximally between these clamps (fig. 4), the rectosigmoid being thus removed with the tumor within it. A small rubber drain is inserted on either side of the ends of bowel, and the tissues are loosely approximated around the ends of bowel and the drains. The anal purse string suture is removed. The crushing clamps are left in place for

forty-eight hours, after which they are removed, and a few days later the right angle clamps (fig. 5) are placed in the usual way to cut through the septum separating the intestinal lumens. These slough out a few days later, and the sacral wound granulates in, the continuity of the bowel being reestablished. As an alternative, the loop of bowel containing the carcinoma may be left protruding through the sacral incision and may be severed between clamps at a later date; this gives the sacral wound time to heal partially before it is contaminated with fecal material. A piece of rubber dam is thrust up between the mobilized terminal portion of the sigmoid flexure and the sacrum and is left protruding through the sacral incision for drainage.

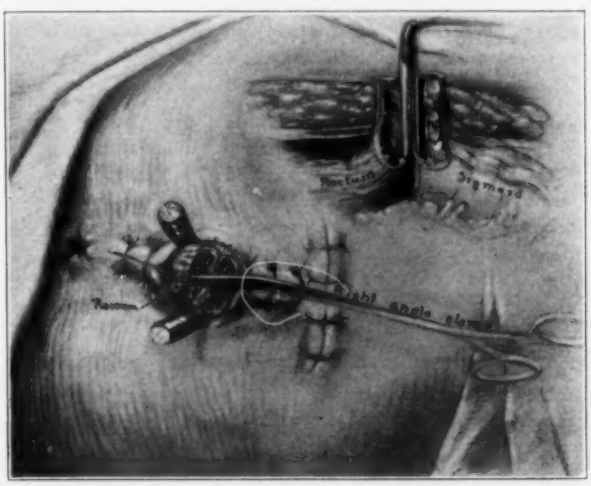

Fig. 5.—Right angle crushing clamp on the intestinal septum. The insert is a side view of the clamp in place, with part of the bowel cut away. If one desires to remove a larger segment of the intestinal septum two clamps may be used, placed about ½ inch (1.2 cm.) apart.

REPORT OF A CASE

I have performed this operation in only 1 case, with the following result:

A man aged 59 had well advanced annular adenocarcinoma of the rectosigmoid. He was in good physical condition. The blood pressure was normal. All the organs were normal on routine examination. Routine laboratory examination showed nothing of note. The rectosigmoid was not particularly fixed. The abdomen was opened, and no evidence of metastasis was found. The operation was performed as has been outlined. The patient rallied normally from the operation. Forty-eight hours later the two colostomy clamps were removed, and immediately the two right angle crushing clamps were applied. On the third day fecal material came through the proximal colostomy opening, and on the fourth day the patient was passing gas. The ends of the bowel showed good color. The sacral wound continued to look healthy, and the right angle clamps came off a few

days later. On the eighth day the sacral wound was only about the size of a half-dollar. A rectal tube was inserted through the anus, well up above the sacral opening and into the sigmoid flexure. This part of the operation was satisfactory. On the third, fourth and fifth days there was some abdominal distention, which subsided on the fifth day and did not return. The abdomen thereafter showed nothing of note. On the fourth day an infection of the thorax developed, which gradually became worse. There was a large amount of mucus, and considerable dyspnea was noted. A roentgenogram of the chest on the eighth postoperative day showed the lungs infiltrated with numerous minute round opaque areas. There was some roentgen evidence of edema. The left side of the heart was hypertrophied. The patient died of the thoracic infection on the ninth postoperative day, but the result of the operation had been normal. It is a matter of conjecture whether this patient's life would have been saved by a multiple stage operation.

Autopsy.—Autopsy failed to show any evidence of metastasis in the abdominal cavity. The liver, spleen, kidneys and mesentery were normal. There was no evidence of peritonitis. All the peritoneal suture lines were in good condition. There was no evidence of obstruction in the descending colon, and the color of the sigmoid flexure was normal down to the colostomy opening. No part of the operative area showed the least evidence of a flaw. The heart was somewhat hypertrophied; the lungs were edematous, and the lower lobe of the right lung was collapsed. The lungs showed pneumoconiosis throughout, and microscopic sections showed widespread bronchopneumonia.

COMMENT

By the usual sacral resection of the rectosigmoid it is extremely difficult and sometimes impossible to pull enough of the terminal portion of the sigmoid flexure down to resect satisfactorily the rectosigmoid and reestablish intestinal continuity. By mobilizing the terminal portion of the sigmoid flexure and the rectosigmoid by the abdominal approach it is usually possible to accomplish this, especially when the Mikulicz technic is used in so doing, since less bowel is needed for this purpose than when an end to end anastomosis is undertaken in such a small space. For an end to end anastomosis the bowel must be delivered through the incision. This necessitates access to a considerable length of bowel, which is not necessary for the Mikulicz anastomosis. By the Mikulicz principle a wider resection of the diseased bowel is possible. Suturing the bowel at this site is unsatisfactory, there being a tendency to nonunion and later to stricture formation.

This operation can justly be objected to on the ground that a sufficient portion of the mesosigmoid is not removed. In a given case one may decide at the operating table, with the patient's abdomen open, that a larger part of the mesosigmoid should be removed and may proceed with one of the conventional types of abdominoperineal operation followed by permanent abdominal colostomy. In a case in which the pelvic portion of the colon cannot be sufficiently freed to permit the procedure outlined one makes any one of the permanent types of colostomy opening. In all instances in which the procedure outlined

can be followed it is possible to clear away the node-bearing tissues around the prostate gland and the seminal vesicles or those on the posterior vaginal wall, the cervix and broad ligament. On the other hand, with such a procedure one must risk involvement of the anal and perianal tissues in the spread of the carcinoma. If, however, it is decided beforehand that the growth encroaches too much on the tissues surrounding the anus or if the anal area is involved in the growth or its metastases, naturally permanent colostomy is done, with the removal of all the lower portion of the bowel and the anus, unless one cares to establish a sacral anus. With my operation, abdominosacral resection of the rectosigmoid with the Mikulicz principle of anastomosis through the sacral incision, there is almost no chance of peritonitis, since the bowel is not opened in the abdominal cavity. The sacrum is peculiarly immune to infection. If the operative risk is poor the sacral resection can be left for a later date, since the circulation to this portion of the bowel is not materially interrupted. If one chooses to delay sacral resection, a rubber dam is tucked well down to the coccyx between the sacrum and the mobilized distal portion of the sigmoid flexure and the rectosigmoid, and at the close of the operation a corner of the dam is drawn out through an incision made alongside the coccyx for drainage, as described by Smith.[2] If resection of the exteriorized rectosigmoid is left for a still later date the procedure becomes a three stage operation.

Babcock[3] has devised an operative treatment for resection of the carcinomatous rectosigmoid in which he eliminates the abdominal colostomy, substituting formation of a sacral anus. He has claimed good functional results by this method owing to improvement in the technic and in the viability of the bowel used. He has stated that in the earlier attempts at formation of a sacral anus the end of the sigmoid flexure brought to the perineum sloughed for some distance into the pelvic cavity and left a cicatricial opening that was the source of much later trouble. By his method, with the preservation of the blood supply of the segment of sigmoid flexure brought through the perineum, necrosis of the bowel does not occur, and with an ample opening there is little chance for stricture, so that the bowel empties completely. In some instances he has attempted to obtain a measure of intestinal control by a secondary plastic operation on the sacral anus. In other cases, at a second operation he has split the anal ring anteroposteriorly, dissected away the mucosa, freed the sigmoid-sacral anus and pulled

2. Smith, D.: Two-Stage Procedures in Abdominoperineal Resection of the Sigmoid and Rectum for Cancer, Tr. Am. Proct. Soc. **33**:103, 1932.

3. Babcock, W. W.: The Operative Treatment of Carcinoma of the Rectosigmoid with Methods for the Elimination of Colostomy, Surg., Gynec. & Obst. **55**: 627 (Nov.) 1932.

it down through the sphincters to reestablish a normal anus. This is essentially the Hochenegg technic. In some instances the intestinal lumens have been connected by removal of the intervening tissues at a later operation. In the abdominal part of the operation Babcock does a wide dissection, ligating the sigmoid and the superior hemorrhoidal artery, dividing the mesosigmoid high in its course, and removing all the peritoneum from the bifurcation of the common iliac arteries down to the bottom of the pelvic cavity. He makes no attempt to peritonealize this large denuded area or to form a new pelvic floor. Owing to the ligation of the blood supply to the lower portion of the sigmoid flexure and the high division of the mesosigmoid, it is necessary to pull a large part of the sigmoid flexure down through the sacral incision and amputate it at a high point. This is not always possible or desirable, since in many cases carcinoma of the rectosigmoid remains strictly localized for some time, and wide dissection of tissues is not necessary. On the other hand, a sacral colostomy opening is not as desirable as the normal anus. When the carcinoma involves the anus and surrounding tissues or the portion of the rectum which is below the rectosigmoid, I believe Babcock's method is preferable to permanent abdominal colostomy if good functional results can be obtained. However, in such a case a less extensive abdominal dissection and the establishing of a new pelvic floor with a permanent colostomy opening might be a better procedure. Alternatively, Babcock's extensive abdominal dissection could be combined with the Mikulicz type of anastomosis through the sacral incision.

The old Kraske operation is familiar to all surgeons. It includes removal of a portion of the sacrum, mobilization and amputation of the rectum and the rectosigmoid juncture and formation of a sacral anus or end to end anastomosis. Kraske also devised, later, a combined abdominoperineal operation, freeing the rectum and the sigmoid flexure from above and following this procedure with sacral amputation of the bowel. Quénu and others quickly saw the merit of this method and became ardent advocates of the combined procedure. In a few instances the carcinomatous bowel has been resected and anastomosis done, the anus being left intact. The terminal opening in the sigmoid flexure has been disposed of in a variety of ways by different surgeons.

There are numerous combined abdominoperineal methods for resection of the lower portion of the sigmoid flexure, the rectosigmoid and the rectum, with permanent abdominal colostomy; these include the methods of Miles, Coffey, Lahey, Jones, Rankin and many others.

With the method described by me a cecostomy could be done prior to or coincidentally with the abdominal part of the operation. This would prevent early soiling of the sacral field.

Any surgeon treating carcinoma of the rectosigmoid should have at his disposal many different operative procedures. No one method can be used to the exclusion of all others, since patients present themselves in varying stages of the disease. The two extremes, the abdominoperineal route and the perineal route alone, are represented by the work of Miles, who uses the abdominoperineal route almost to the exclusion of all others, claiming a high percentage of recurrence with the perineal route alone, and by the work of Lockhart-Mummery, who has abandoned all methods except the perineal one, claiming that the difference in recurrence of the growth with the two methods is negligible and that practically as much tissue can be removed by the perineal as by the abdominoperineal route.

My method is also applicable in cases of tumor of the lower portion of the sigmoid flexure in an early stage and too low to be resected from above with anastomosis of the bowel. It can be applied to any operable benign lesion of the lower portion of the sigmoid, the rectosigmoid and the upper part of the rectal ampulla, provided of course, too short a mesosigmoid does not preclude proper mobilization of the bowel.

I believe that the peace of mind of the patient is as important in many instances as his health or even his life. I believe that few, if any, more patients would die after the use of my method than after the use of the abdominoperineal method with removal of a larger portion of the mesosigmoid and permanent abdominal colostomy. Any disadvantage the method may have is overshadowed by the great advantage of a naturally situated anus.

CONCLUSION

A method is described for resection of the carcinomatous rectosigmoid by a combined abdominosacral technic, the Mikulicz procedure being used to reestablish the continuity of the bowel through the sacral incision.

450 Sutter Street.

CARCINOMA OF THE LIP

CLINICAL AND PATHOLOGIC STUDY OF THREE HUNDRED AND NINETY CASES, WITH REPORT OF FIVE YEAR CURES

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There have been many studies and reports on carcinoma of the lip since the publication of the paper of Broders [1] in 1920 on the grading of tumors. However, on reviewing the more recent literature, one finds little accord among surgeons, radiologists and dermatologists on the methods and results of treatment. This may be because both operation and irradiation are satisfactory methods of treatment provided sufficient skill and knowledge are used. The purpose of this paper is to report a rather large series of cases followed beyond the five year period, in which the tumors were treated by surgical operation, and to emphasize the necessity for routine microscopic examination. A comparison is made with the other accepted forms of treatment, that is, irradiation and cauterization. It is difficult to make a true comparison of results, however, because of differences in duration, severity and size of the lesions reported in the literature and the varying periods during which the cases have been followed.

Five year follow-ups have been used as the best index to the results of treatment. The disadvantage of selecting a shorter period has been well borne out in this study, for a number of patients have shown recurrence or metastasis two to four years after treatment, and several four to seven years later. One patient had a recurrence twenty years later. This is contrary to the opinion of Kelly,[2] MacMahon [3] and others, who concluded that recurrence after two years is almost nil in cases of carcinoma of the lip.

The 390 cases forming the basis of this study were obtained from the records of the surgical pathologic laboratory of the Johns Hopkins

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* William Stewart Halsted Fellow in Surgery, 1937-1938.

From the Department of Surgery, the Johns Hopkins Hospital and University.

1. Broders, A. C.: Squamous Cell Epithelioma of the Lip, J. A. M. A. **74**: 656 (March 6) 1920.

2. Kelly, E.: Radium Therapy in Carcinoma of the Lip, J. A. M. A. **100**: 388 (Feb. 11) 1933.

3. MacMahon, J. S.: Squamous Cell Carcinoma of the Lip, Australian & New Zealand J. Surg. **7**:40 (July) 1937.

Hospital from 1900 to 1933. The diagnosis of carcinoma has been made in every instance from the sections, except in 10 of the earlier cases (all cases of hopeless cancer). This is likewise true of the cases in which metastasis occurred. The lesions dealt with in this report were, in general, fairly well advanced. Besides affecting the percentage of five year cures unfavorably, the delay in treatment shows the need for more prompt attention to lesions of the lip. The percentage of patients who showed metastasis or recurrence on first examination (36.4 per cent, or 143 of 390 patients) indicates the delay in diagnosis and treatment. The average duration of symptoms was in excess of two years. Kennedy,[4] from New York, reported 33 per cent with metastasis among the 98 patients on whom dissection of the cervical glands was done, while clinically 60 per cent of the patients had palpable glands. Broders at the Mayo Clinic found metastasis in 24 per cent of the patients on whom dissection of the cervical glands was done. Kelly, of Baltimore, however, in his series of 252 cases found that only 14 per cent of patients had palpable cervical glands on admission. He also reported another group, representing 20 per cent of his series, who previously had been treated by operation or irradiation elsewhere, but the incidence of metastasis in this group is not stated. MacMahon, from the Royal Prince Albert Hospital in Sydney, Australia, reported 10.3 per cent of patients with cervical metastases in 299 cases in which dissection of the cervical glands was performed.

CLINICAL FEATURES

The lesion first noticed by most of the patients was a small, painless ulcer, which at first grew slowly. Scabs often formed, and the lesion sometimes healed before a raw area reappeared. Frequently the patients stated that they had had fever blisters before, but that this time the fever blister did not heal. The lesions usually became worse after the use of salves and mild caustics, although there was seldom any associated pain. Other early lesions noted by the patients were warts, cracks, fissures, leukoplakia and chapping of the lips.

In regard to the etiologic factors, an attempt was made to note the relation of carcinoma of the lip to smoking, poor oral hygiene and exposure to the wind and sun. No satisfactory statistical evidence was found, but it seems evident, as emphasized by Bloodgood[5] and others, that chronic irritation in the form of the factors mentioned plays a definite

4. Kennedy, R. H.: Epithelioma of the Lip with Particular Reference to Lymph Node Metastases, Ann. Surg. **99**:81 (Jan.) 1934.

5. Bloodgood, J. C.: Lesions of the Oral Cavity and of the Jaws, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1930, vol. 4, chap. 4.

Fig. 1.—Photograph of a man aged 51 with a typical squamous cell carcinoma of the upper lip of three months' duration. A V excision of the lip was done. The patient was well seven years later. There was no recurrence.

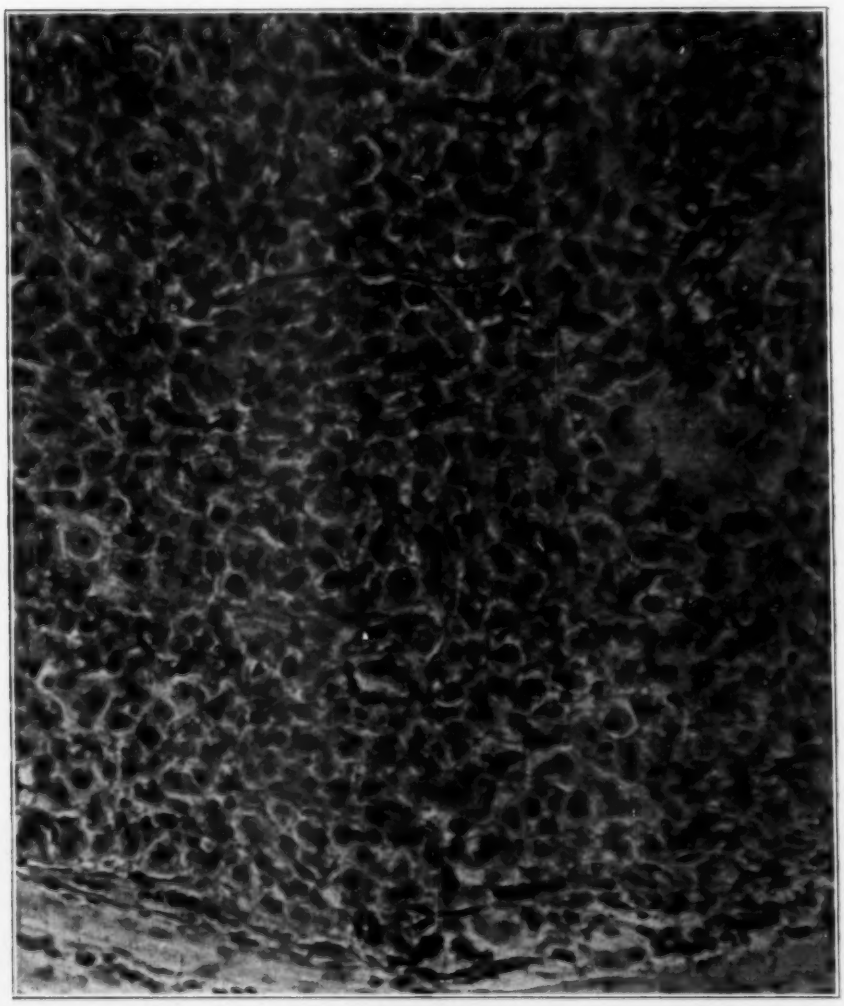

Fig. 2.—Low power photomicrograph of the lesion illustrated in figure 1. Notice the lack of pearl formation and the invasive character of the squamous cells.

part, although it is by no means the sole cause. A study of the occupations of the patients showed the greatest number to be farmers. The hygienic condition of the mouth was poor in the vast majority of cases, many patients having a positive test for the organisms of Vincent's angina. Dirty, ragged, tobacco-stained teeth were noted frequently. In 2 cases carcinoma of the lower lip developed at the site of trauma from a ragged upper tooth.

TABLE 1.—*Age Incidence of Carcinoma of the Lip*

	Age, Years						
	20-30	30-40	40-50	50-60	60-70	70-80	80-90
Lower lip							
Squamous cell carcinoma	3	25	50	74	68	31	4
Malignant warts (papillary carcinoma grade)	0	3	9	10	11	7	1
Basal cell carcinoma	0	0	2	2	2	1	0
Upper lip							
Squamous cell carcinoma	0	2	1	4	5	1	0
Basal cell carcinoma	0	2	4	10	10	3	0
Adenocarcinoma	0	0	0	1	1	0	0

TABLE 2.—*Statistics on Carcinoma of the Lip*

	Number of Cases	Sex of Patients		Average Age, Years	Average Duration of Lesion, Months	Condition on Admission		
		Males	Females			No Metastasis	Metastasis	Recurrences
Lower lip								
Squamous cell carcinoma (grade 2, 3 and 4)	281	276	5	55.9	28.1	151	103	27
Malignant wart (papillary carcinoma)	47	46	1	57.1	30.8	47	0	0
Basal cell carcinoma (all grades)	8	8	0	57.2	46.1	8	0	0
Upper lip								
Squamous cell carcinoma (all grades)	16	12	4	54	20	12	1	3
Basal cell carcinoma (all grades)	36	23	13	57	28	27	0	9
Adenocarcinoma (all grades)	2	2	0	60	3	2	0	0

Tables 1 and 2 summarize some of the important statistics on carcinoma of the lower and upper lips, based on the cases studied. The age incidence agrees well with that of other published reports. The duration of the lesion before examination varies considerably. The average time in this series is a little over two years. This gives a somewhat false impression, because it also includes the patients who have been treated previously by improper methods. In many instances, when the patient stated that the lesion had been present five, ten or fifteen years, it was found that actually a benign lesion had been present during

this period, and on careful questioning the patient admitted that there had been very little, if any, growth during this time and that only in the past few months (not more than twelve) had growth and destruction really occurred.

The relation to sex and race is interesting, although the latter is not adequately represented because of the large number of Bloodgood's private patients included in this series. Less than 1.5 per cent of the 390 patients were Negroes. Only 1.8 per cent of carcinomas of the lower lip occurred in women, while for carcinoma of the upper lip the percentage was much higher, 45.9 per cent of these lesions occurring in women.

Mention has already been made of the number of cases in which metastasis occurred. Of the total number of 390 cases, 143 presented metastasis, recurrence or both on the patients' first admission to the hospital, as shown by microscopic examination. In table 2, under the heading "Metastasis" are included both lesions with metastasis and lesions with recurrence plus metastasis. In the group under the heading "Recurrences," only recurrent lesions are included in which there were no metastases on first admission. A discussion of cases in which the lesions were arrested beyond the five year period will be presented later, when treatment is considered. No mention has been made of the size of the tumor, although it is evident that this is an important consideration. The various descriptions as to the size were usually estimations, so that no statistical report of the size of the lesions could be made.

PATHOLOGIC PICTURE

In the series of 390 cases, there were 344 cases of squamous cell carcinoma, 44 cases of basal cell carcinoma and 2 cases of adenocarcinoma. The incidence of basal cell carcinoma of the lower lip is 2.1 per cent and that of basal cell carcinoma of the upper lip is 66.6 per cent. The incidence of basal cell carcinoma of the lower lip is probably lower than this, as this includes basal cell lesions which involved the lip at the time of examination but which the patient thought had begun just below the vermilion border. Among lesions of the upper lip, carcinoma on the cutaneous side of the upper lip was included.

The term "malignant wart" has been used to indicate the low grade papillary type of squamous cell carcinoma, and such a growth is equivalent to a grade 1 carcinoma of Broders' classification. This is the classification previously adopted by Bloodgood. No attempt has been made to reclassify the cases according to Broders' method of grading, although after a study of the sections in this series it is evident that the degree of microscopic differentiation is of value both in the selection of treatment and in prognosis, when used in conjunction with the dura-

tion and extent of the disease, as MacCarty and Broders recommended. Determination of the type of carcinoma (whether basal cell or squamous cell) is of great value, as is well known, in prognosis. There was no case of basal cell metastasis in this series, although recurrences did take place.

There are recorded in the surgical pathologic laboratory a number of benign lesions of the lip which were clinically diagnosed as malignant and a number of early malignant lesions in which the clinical impression was that of a benign lesion. This is ample evidence that a microscopic study should be made of all questionable lesions of the lip for which carcinoma is considered a possible diagnosis. In figures 3, 4 and 5 are shown three lesions of the lip. The lesions in figures 3 and 4 were carcinomas, and that in figure 5 was a benign wart. These three pictures were shown to four clinicians, who were requested to state which lesions they thought were malignant. In every instance the lesion in figure 5 was pointed out as a malignant instead of a benign lesion and that in figure 4 as a benign instead of a malignant lesion.

This emphasis on microscopic examination for carcinoma of the lip has also been made by many other authors, among whom are Hyndman,[6] Kennedy,[4] Martin,[7] Figi [8] and Richards.[9] Hyndman in particular stated that the microscopic appearance is of great value in determining the necessity of removing or irradiating the cervical glands. This is also the tendency at the Mayo Clinic, where dissections of the neck are done routinely for grade 2, 3 and 4 carcinoma of the lip (Claude F. Dixon).[10] At the Johns Hopkins Hospital, irradiation and surgical treatment are now both used, but when surgical treatment is used and the microscopic picture is that of a malignant wart (grade 1 carcinoma, Broders) the cervical glands are not removed.

RESULTS OF TREATMENT

During the period under consideration, 390 patients sought treatment. Of that number, 349 were given surgical treatment; 24 presented hopeless lesions and were treated with palliative measures; in 13 there

6. Hyndman, O. R.: Carcinoma of the Lip with a Clinicopathological Analysis of Seventy-Seven Cases, Arch. Surg. **27**:250 (Aug.) 1933.

7. Martin, H. E.: Treatment of Cancer of the Lip, Am. J. Surg. **30**:215 (Nov.) 1935.

8. Figi, F. A.: Epithelioma of the Lower Lip, Surg., Gynec. & Obst. **59**: 810 (Nov.) 1934.

9. Richards, G. E.: Radiological Treatment of Cancer of the Lip, Canad. M. A. J. **35**:490 (Nov.) 1936.

10. Dixon, C. F.: Submental and Bilateral Submaxillary Dissection, S. Clin. North America **15**:1303 (Oct.) 1935.

Fig. 3.—Photograph of a man aged 56 with a squamous cell carcinoma of six months' duration. A V excision of the lip was done. The patient died two years later of angina pectoris. There had been no recurrence of the carcinoma.

Fig. 4.—Photograph of a man aged 46 who had carcinoma of the lip of three months' duration. The clinical impression was benign tumor. A V excision of the lip was done. There was local recurrence eight years later of a similar low grade squamous cell carcinoma.

Fig. 5.—Photograph of a man aged 66, with a benign squamous cell wart of one year's duration. The clinical impression was malignant wart. A V excision of the lip was done. The patient was well three years later. There was no recurrence.

were insufficient data for classification, and 4 patients with early carcinoma received primary irradiation treatment. The total number of patients followed over a period of five years or more was 328. Of that number, 181 lived for a period of five years, 114 died from carcinoma

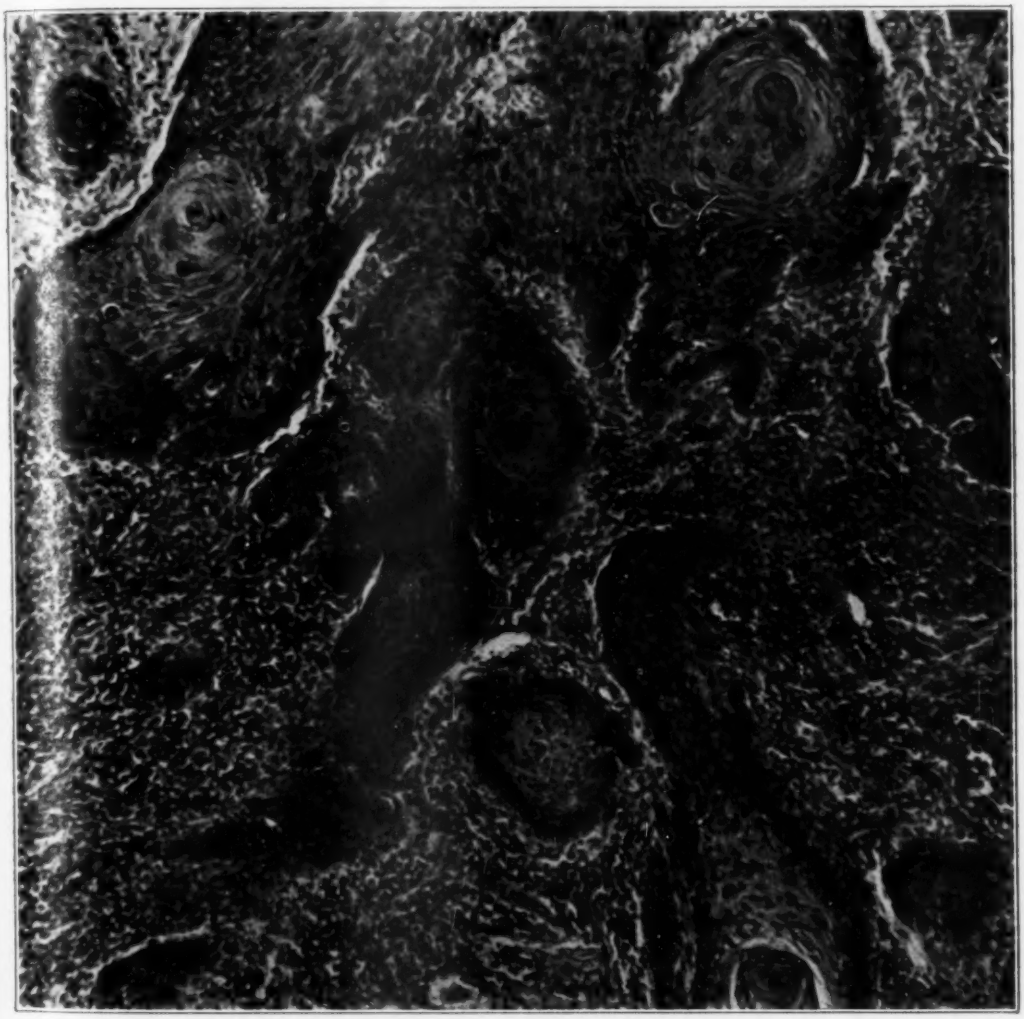

Fig. 6.—Low power photomicrograph of the lesion shown in figure 3. Note the invasive character of the epithelial cells at the base of the ulcer and the tendency to pearl formation.

and 34 died of some intercurrent disease within the five years and are excluded from all statistics. Thus, the percentage of five year cures for the 328 patients (including patients with hopeless cancer) is 61.6 per cent.

The cases have been divided into as few groups as possible, so that a sufficient number will have been followed in each group to make the statistics as accurate as possible. In table 3 the cases have been divided into three groups, according to treatment received. Group 1 consists of 176 cases in which there was no evidence of metastases clinically and in which only excision of the tumor of the lip was done. After the 17

Fig. 7.—Low power photomicrograph of lesion seen in figure 4. Note the carcinoma beginning at the base of the lesion. This is illustrated better in a high power photomicrograph.

cases in which the patients died of some intercurrent condition were deducted, the percentage of five year cures in the 149 cases traced was 80.9. Group 2 consists of 90 cases in which the tumor was excised, dissection of the cervical glands performed and no metastasis found. Of this group 85.3 per cent of the 80 patients traced were well after five years. At first glance one might conclude that the method employed

for group 2 is the best procedure to follow in the treatment of cancer of the lip in the early stages, but it must be remembered that the two groups are not identical. It is possible that in 2 or 3 cases in group 1 metastasis may have been present when the tumor was excised. Also 1 case is included in group 1 in which dissection of the glands of the neck was advised but permission was refused, and metastasis and death occurred.

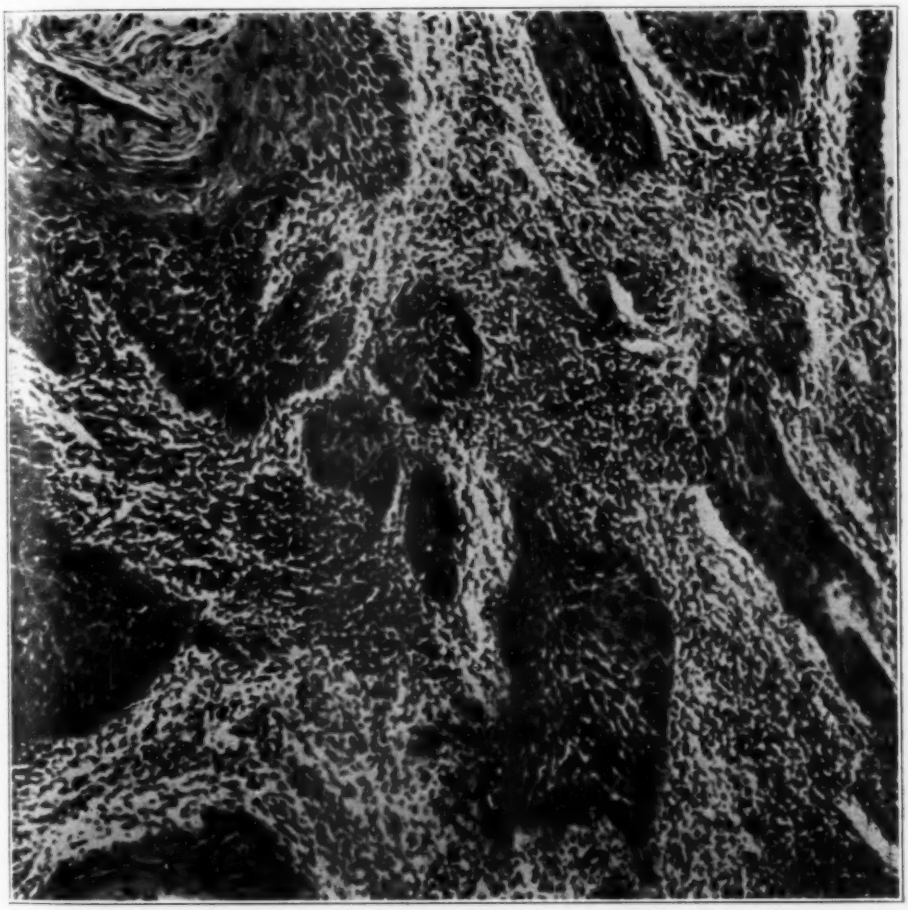

Fig. 8.—Low power photomicrograph of the recurrent lesion shown in figure 4 and figure 7.

However, even with this slight inequality in comparison, the patients in the cases of group 2 were, by and large, "poorer risks" than those in group 1, so that dissection of the cervical glands in certain selected cases seems to be the best procedure. Just what the criterion should be it is difficult to state, but for patients with clinically palpable glands or with

a highly invasive type of carcinoma (grade 3 or 4) it would seem advisable to perform dissection of the cervical nodes.

Group 3 consists of 83 cases in which metastases were found. In this group radical excisions, including cervical dissections and plastic

Fig. 9.—Low power photomicrograph of the benign wart shown in figure 5. The basement membrane is intact, and there is marked leukocytic infiltration. However, there is no change in the size or character of the epithelial cells.

repair when necessary, were performed. The operative mortality was chiefly in this series, 8 of the 13 operative deaths occurring in group 3 and 4 in group 2. An additional operative death was that of a patient

excluded from classification because of insufficient data. The percentage of five year cures in this group is low, 22.5. This emphasizes again the importance of early treatment of carcinoma of the lip.

One of the first impressions formed in this study was the large number of patients who had been previously treated with caustics, roentgen therapy or radium therapy. There were 66 such patients with involvement of the lower lip in this study, and 55 of the 66 presented metastasis or extensive recurrence on first admission. This is not an attempt to point out the inefficiency of irradiation, but to bring out the

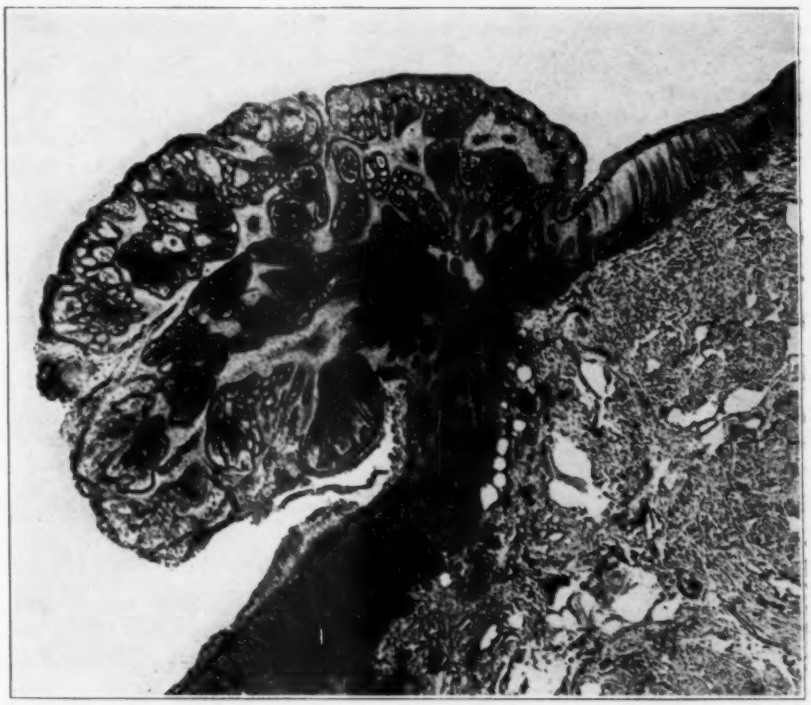

Fig. 10.—Very low power photomicrograph of the benign lesion shown in figures 5 and 9. This shows very well the character of the entire wart.

fact that irradiation is not used in general practice with the same skill with which it is used in the larger clinics. This has also been emphasized by Figi in a recent study from the Mayo Clinic; he found the percentage of five year cures lower in his cases of secondary growth (previously treated by insufficient roentgen therapy, radium therapy and caustics), and a higher degree of malignancy and metastasis.

In table 4 is given a comparison of cases taken at random from the literature, to show the five year results of various forms of treatment. An attempt has been made as far as possible to choose similar cases,

although the groups are not absolutely identical. In the group taken from the department of surgical pathology at the Johns Hopkins Hospital, all the cases in which only local excision was done and the cases in which dissection of the cervical glands was done but no metastasis was found have been included. The same is true of the series which

TABLE 3.—*Treatment*

Type of Treatment*	Number of Cases	Number Cases Traced for 5 Years	Percentage of 5 Year Cures
Group 1. Excision of tumor only (no metastasis clinically)	176	149	80.9
Group 2. Excision of tumor and dissection of cervical glands (no metastasis)	90	80	85.3
Group 3. Radical excision and dissection of cervical glands (metastasis present)	83	75	22.5
Operative mortality	3.7 per cent; 13 deaths in 349 surgical cases		
Hopeless (inoperable) carcinoma	6.1 per cent; 24 of 390 cases		
Operation	349		
Irradiation (primary treatment)	4		
Hopeless (palliative treatment)	24		
Insufficient data	13		
Total number of cases	390		

* In 11 of the total 349 surgical cases postoperative irradiation therapy was given.

TABLE 4.—*Treatment of Carcinoma of the Lip*

Type of Treatment	Number of Cases Treated	Traced for 5 Years	Percentage of 5 Year Cures
Operation; all grades of cancer but no metastasis on first admission (Johns Hopkins Hospital)	266	228	82.4
Operation; primary treatment (no previous treatment) (Figi, Mayo Clinic)	...	217	80.3
Operation; primary treatment (no previous treatment) on first admission (MacMahon, Royal Prince Albert Hospital)	351	228	90.3
Radium; primary treatment(no previous treatment) (MacMahon, Royal Prince Albert Hospital)	215	70	82.7
Radium; early cancer with no metastasis (Kelly-Kelly Radium Clinic)	...	67	81.7
Local destruction with or without irradiation; early cancer with no metastasis (Wile and Hand, Univ. of Michigan Clinic)	...	49	53.8

received surgical treatment from the Royal Prince Albert Hospital in Sydney, Australia. No explanation is necessary for the other series which received irradiation and local destruction. The number of cases in which irradiation of the regional lymph nodes as well as of the primary lesion was given could not be definitely determined, but undoubtedly a considerable number of such cases existed.

The interesting points in the comparison are the good results obtained by operation and the uniformity of results obtained by MacMahon from

the Royal Prince Albert Hospital with the results of radium therapy reported by Kelly and the surgical results reported in this paper and by Figi from the Mayo Clinic. Whether the slightly better results obtained by operation is of any practical value as far as treatment is concerned, is questionable. MacMahon concluded that it is a sufficient difference. What statistics do not show but what seems important is that there is apt to be more uniformity of treatment by operation than by radiation. This seems logical because the knowledge, experience and skill necessary to calculate the proper dose of radiation is greater than that necessary for surgical excision with a sufficient margin of normal tissue. Another factor in favor of surgical treatment is that the whole specimen is obtained for microscopic study, so that a more accurate determination can be made as to prognosis and the need of further therapy. For a large superficial lesion involving both sides of the lip irradiation may be an easier procedure and may offer a better cosmetic result.

TABLE 5.—*Types of Carcinoma*

Type	Number
Carcinoma of the stomach	2
Carcinoma of skin, other than lip	2
Carcinoma of the tongue	1
Carcinoma of the esophagus	1
Carcinoma of the liver	1
Carcinoma of the penis	1
Carcinoma of the jaw	1
Total	9

No discussion has been given concerning treatment by dermatologic methods. The results reported by different observers [11] in the dermatologic field are too variable to permit conclusions regarding the value of cauterization. It is apparent, however, that with this method as with insufficient irradiation, recurrence is common and renders the prognosis with further treatment poor.

DEATH DUE TO OTHER CAUSES

During the five year period following treatment, there were 34 deaths due to intercurrent diseases in the 328 cases followed. The more common causes of death in their order of frequency were: cardiac disease, cerebral hemorrhage, disease of the kidneys, pneumonia, senility, injury, intestinal obstruction and jaundice.

11. Wile, U. J., and Hand, E. A.: Cancer of the Lip, J. A. M. A. **108**:374 (Jan. 30) 1937. Elliott, J. A.: Treatment of Epithelioma of the Lip by the Dermatologist, Arch. Dermat. & Syph. **27**:373 (March) 1933.

It is interesting to note the number of patients in whom carcinoma developed elsewhere in the body after treatment for carcinoma of the lip. In the series of 328 patients followed, 9 eventually showed other forms of cancer.

COMMENT

When this study was undertaken, there were three questions which were of interest to me. They were: Is operation a satisfactory way to treat carcinoma of the lip? Is dissection of the cervical glands of real value as a prophylactic measure? Why is there so much apparent disagreement as to the proper way to treat carcinoma of the lip? The last question is satisfactorily answered by the fact that good results are now being obtained by both operation and irradiation for carcinoma in early stages. The second question is slightly more difficult. However, it would seem from the results in this series that in a selected group of cases in which the tumor showed a high grade of malignancy and invasion of the deeper structure of the lip, with or without clinical evidence of metastasis, dissection of the glands of the neck is a wise procedure. The answer to the first question is not difficult, for the results show that operation is a method of treating carcinoma of the lip which is as desirable as radium therapy or cauterization, and that the percentage of five year cures may perhaps be slightly higher.

SUMMARY

A clinical and pathologic study of 390 cases of carcinoma of the lip is presented. The diagnosis has been made from the microscopic examination in all except 10 cases, all cases of hopeless carcinoma.

Statistics are given (table 2) as to the number of cases, type of carcinoma, age incidence, sex of the patient, average duration of the lesion, the presence or absence of metastasis or recurrence when the patient was first examined.

There were 344 cases of squamous cell carcinoma, 44 cases of basal cell carcinoma and 2 cases of adenocarcinoma. Only 2 per cent of the basal cell lesions occurred on the lower lip, and none of the adenocarcinomas.

There were 336 malignant lesions of the lower lip and 54 malignant lesions of the upper lip.

"Malignant wart" is a term used to indicate the papillary, squamous cell, low grade type of carcinoma.

Illustrations are shown (figs. 3, 4 and 5) to emphasize the fact that clinically a lesion cannot always be diagnosed as benign or malignant. Emphasis is put on the microscopic study in relation to prognosis and therapy.

Five year follow-ups were selected as the best index to results obtained in treatment. Follow-ups were obtained in 328 of the 390 cases. The percentage of five year cures for the entire series was 61.6.

The incidence of metastasis or recurrence on first examination was 36.4 per cent.

The results of treatment are reported for three groups; group 1, in which local excision alone was performed on 176 patients with no clinical evidence of metastasis, showed 80.9 per cent of five year cures. Group 2 included cases in which local excision plus dissection of the cervical glands was carried out, but no metastasis found microscopically. The percentage of five year cures in group 2 was 85.3. Group 3 consisted of 83 cases in which both local excision and cervical gland dissection were done, in which metastasis was found. The percentage of five year cures in group 3 was 22.5.

The operative mortality was 3.7 per cent in 349 cases; 8 deaths occurred in the more radical operations necessary in group 3, 4 deaths occurred in group 2. No operative deaths occurred in group 1.

In table 4 is given a comparison of five year results from the literature in patients treated by operation, irradiation and dermatologic methods. In this comparison, operation compares favorably with the other methods of treatment.

EPULIS

A SERIES OF CASES

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According to Römer,[1] the term epulis was first employed by Galen to designate a tumor on the gums. The term as used by him applied generally to any kind of abnormal gingival growth. In more recent times its use has been restricted, as a rule, to certain types of growth found in this region of the oral cavity, although some writers still use the word in its more general meaning.

This report records observations on a series of cases of epulis and does not pretend to discuss the proper use of the term or the kinds of tumor that might be included under it. As used here, "epulis" refers to a benign epithelium-covered connective tissue tumor found immediately around the teeth and having its origin in the pericementum or the periosteum of the marginal alveolar process.

The tumor will be described from the standpoint of (1) clinical manifestations, (2) clinical diagnosis, (3) roentgen findings, (4) treatment, (5) results of treatment, including early and later follow-up observations and (6) histologic appearance.

Virchow [2] pointed out that there is a certain convenience in speaking of epulis as sarcomatous, fibromatous or myxomatous. Lukomsky [3] stated that "according to its origin and character, epulis might be called an osteofibroma" and

> In the development of epulides there are two forms which appear different at different times, (1) an earlier complex form with giant cells, and (2) a later pure fibromatous form.

From the Department of Surgery, the Yale University School of Medicine.

Read at the Seventy-Third Annual Midwinter Meeting of the Chicago Dental Society.

1. Römer, O.: Die Epulis, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1938, vol. 4, pt. 2, p. 432.

2. Virchow, R.: Die krankhaften Geschwülste, in Die Cellularpathologie in ihrer Begründung auf physiologische und pathologische Gewebelehre: Zwanzig Vorlesungen über Pathologie, ed. 2, Berlin, A. Hirschwald, 1862, p. 292.

3. Lukomsky, J. H.: Die Epuliden, Deutsche Monatschr. f. Zahnh. **44**:697, 1926.

Thoma [4] stated:

> When they are newly formed they are generally very vascular and red and bleed easily when injured. When of long standing they become more solid and firm, often losing their inflammatory character and changing to fibroma.

Garretson,[5] Blair and Ivy,[6] Rywkind,[7] Häupl [8] and others have differentiated between various types of proposed classifications of epulis based on the predominant type of tissue. In general (fig. 1) the groupings suggested by the various writers include (1) that in which the connective tissue predominates (fibromatous epulis), (2) that in which the vessels predominate (angiomatous epulis) and (3) that in which giant cells predominate (sarcomatous, or benign giant cell, epulis). Although the majority of epulides can be placed under these headings, some are

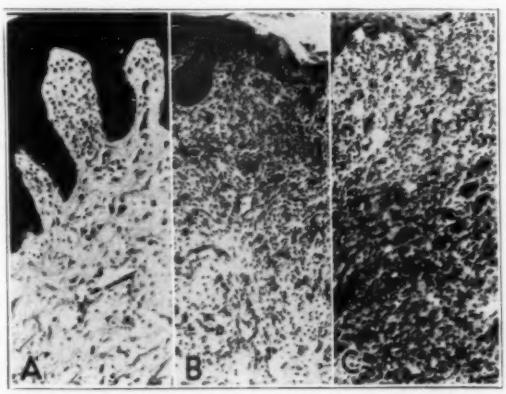

Fig. 1.—Photomicrographs (× 75) of histologic sections of (*A*) an epulis in which connective tissue predominates, (*B*) one in which vessels predominate and (*C*) one in which giant cells predominate.

encountered that do not belong in any of these categories. There are also many variations within each group.

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4. Thoma, K. H.: Peripheral Tumors of the Oral Tissues, in Clinical Pathology of the Jaws with a Histologic and Roentgen Study of Practical Cases, Springfield, Ill., Charles C. Thomas, Publisher, 1934, p. 345.

5. Garretson, J. E.: The Tumors of the Mouth, in A System of Oral Surgery, ed. 2, Philadelphia, J. B. Lippincott Company, 1873, p. 819.

6. Blair, V. P., and Ivy, R. H.: Essentials of Oral Surgery, St. Louis, C. V. Mosby Company, 1925, p. 278.

7. Rywkind, A. W.: Die Epuliden und deren Beziehung zur Ostitis fibrosa, Virchows Arch. f. path. Anat. **263**:415, 1927.

8. Häupl, K.: Zur Kenntnis der sogenannten Riesenzellensarkome der Kiefer, Vrtljschr. f. Zahnh. **41**:449, 1925. Hesse, G.: Die Epulis, Leipzig, A. Pries, 1907.

Probably the only important characteristic that the giant cell epulis has in common with the regular giant cell sarcoma is the formation of giant cells. In the giant cell epulis, which is under consideration here, the giant cells may be many or few and may be scattered throughout the tumor or occur only in focal areas. In this series they occur only in the younger vascular epulides, found in the younger patients.

In the vascular type of epulis also there is considerable variation. In some tumors there seems to be a supply of blood vessels adequate only for normal nutrition. Others may be highly vascular, simulating true hemangioma. The blood vessels may be normal, small or large or may appear in the section as wide endothelium-lined blood spaces. They may be found in focal areas or generally distributed throughout the tumor.

Fibromatous epulis also shows great variation. The connective tissue may be of a uniform dense normal adult type, or young and either loosely woven or interspersed with strands of a more dense type. Some such fibromas contain calcium salts in the form of (1) amorphous deposits of calcium, (2) round calcific masses scattered throughout the tumor, (3) spicules of bone and (4) regular laminated trabecular bone. The epulides containing osseous structures will receive particular attention in this report.

Ten of a group of 20 patients stated that the epulis began with a local mechanical injury. In most of these the injury was caused by a carious or broken-down tooth. The other patients were uncertain as to the beginning of the tumor.

The tumors were removed with the region under local anesthesia, 1 to 3 cc. of 2 per cent procaine hydrochloride with 1 to 3 minims (0.06 to 0.18 cc.) of 1:1,000 epinephrine being used. An incision was made around and 2 to 3 mm. beyond the margin of the tumor through to the underlying hard structures. The entire mass was elevated and removed, and the region of the attachment was thoroughly curetted. A blood clot was then allowed to form, and the patient was dismissed. As a rule it was not necessary to employ sutures. The patients were seen from ten days to two weeks after the operation, satisfactory healing taking place during the interval. Regular instruction in oral hygiene was given, but there was no further postoperative treatment.

Teeth which seemed to be undergoing displacement from their sockets by the growth of the tumor mass were removed, with involved portions of their immediate supporting structures (fig. 2). This operation was performed in 4 of the 20 cases.

In 1 instance the normal eruption of the upper left permanent first incisor had been impeded by the growth of the tumor around the

crown of this tooth and the resorbing root of its deciduous predecessor. Eruption of the permanent incisor into normal occlusion followed the removal of the tumor (fig. 3). When teeth had been merely tilted

Fig. 2.—Photograph, natural size, of an epulis in the left anterior portion of the mandible. The tumor has displaced several teeth by its growth.

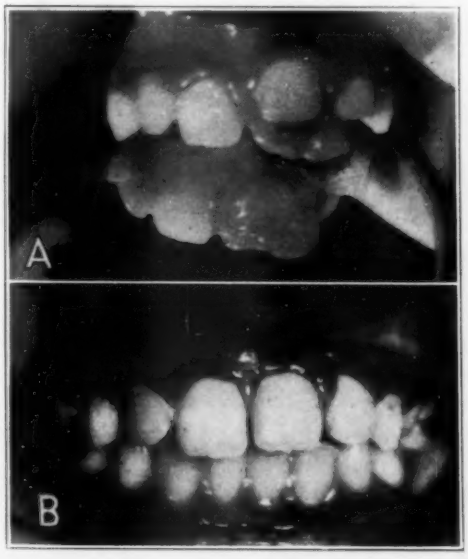

Fig. 3—Photographs, natural size, of (*A*) an epulis in the left anterior portion of the maxilla which apparently prevented the proper eruption of the permanent first incisor; (*B*) the same region one year after the removal of this tumor, showing the teeth in normal occlusion.

out of alinement by the growth, a return to their normal positions in the dental arch followed the removal of the tumor (fig. 4).

Nine of the 20 patients have been followed for less than one year, 1 for between one and two years, 5 for two to three years, 1 for between

Figure 4

Figure 5

Fig. 4.—Roentgenograms of the mandibular permanent incisors, showing (*A*) the positions of these teeth before the removal of a small epulis situated between the crowns of the first two incisors; (*B*) the spontaneously corrected positions of these teeth, observed one year after removal of the tumor.

Fig. 5.—Roentgenograms showing (*A*) the position of the maxillary left second bicuspid and the bony projection into the central portion of an epulis situated in this region; (*B*), the condition one year after excision of the epulis, the second bicuspid and the bony growth.

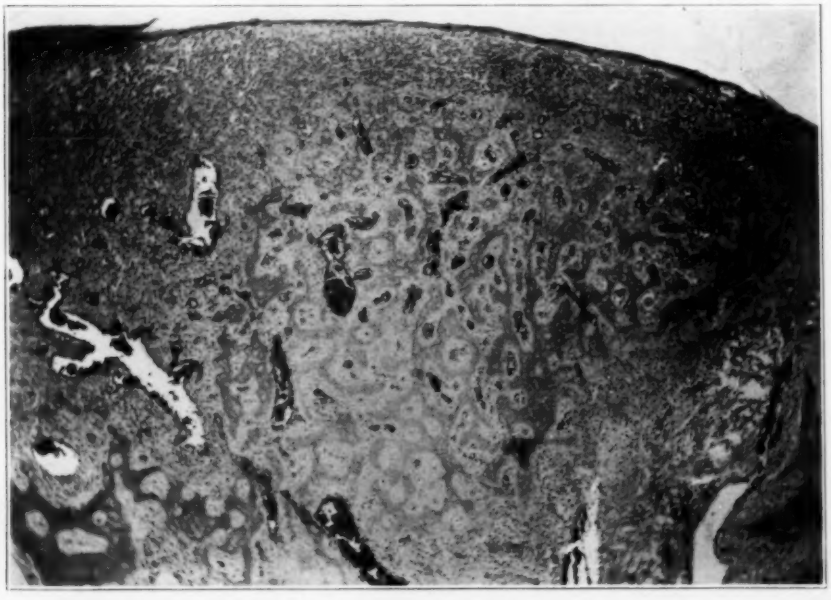

Fig. 6.—Photomicrograph (× 75) of an epulis which had its attachment between the mandibular right second incisor and cuspid. Note the various stages of osseous development, ranging from the earliest signs of calcification to mature bone.

three and four years and 4 for four to five years. No tumor so far has shown any evidence of recurrence.

The histologic preparations showed that 3 tumors in the series of 20 contained giant cells; 7 contained regular laminated trabecular bone demonstrable as a part of the tumor mass, and all showed varying degrees of chronic inflammatory reaction with increased vascularity. In 1 instance the bone occurred as an outgrowth of the alveolar process, providing a firm support for the tumor (fig. 5). In another, various stages of osseous development were observed, ranging from the earliest signs of calcification to the presence of mature bone (fig. 6).

It is of particular interest that osseous structures were present in 6 tumors which, according to the history and physical examination, had been subjected to direct masticatory stress for a year or more. Furthermore, these structures occurred only in patients in the third decade of life or beyond. In 1 instance regular bone was found in one of the older tumors that had not been in occlusion.

SUMMARY

The various types of epulis, classified according to their characteristic histologic structure, may represent different stages of development of the same growth.

In this series only the younger epulides, found in the younger patients, contained giant cells. The older epulides, found only in patients in the third decade of life or beyond, contained regular laminated trabecular bone.

This type of osseous structure in all but 1 instance followed masticatory stress directly to the tumor mass.

The majority of the patients stated that the epulis began with a local mechanical injury to the place of origin.

Indications for the extraction of teeth displaced by the tumor may be determined partly by the direction of displacement.

POSSIBILITY OF DIFFERENTIAL SECTION OF THE SPINOTHALAMIC TRACT

A CLINICAL AND HISTOLOGIC STUDY

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By 1905 Spiller [1] had conceived of an isolated tract in the spinal cord mediating pain. In 1911 Martin,[2] at Spiller's suggestion, did the first chordotomy to relieve pain. This operation, which has come to be known as the Spiller-Frazier operation, or, more commonly, as chordotomy, has been done many times since its introduction, and numerous reports have testified to its efficacy and value.

In doing 41 chordotomies during the past three years, one of us (O. H.) saw reason to question the accepted location of the spinothalamic tract as well as the accepted disposition of its fibers. We are reporting 6 cases in which the operation was done with the patient under local anesthesia only. Sections were made in the cord according to various patterns, and cutaneous sensibility was tested at the operating table.

GENERAL FACTORS RELATED TO CHORDOTOMY

Segment of Election.—The most popular locations for section have been the regions of the first, second and third thoracic segments and the fifth, sixth and seventh thoracic segments, or, more specifically, that part of the cord beneath the second, the third or the sixth laminal arch. All of our sections have been made beneath the second or the third arch, but a lower site has the advantage of not being between the shoulder blades and is satisfactory if the patient's pain is not located higher than the groin.

From the Departments of Surgery and Neurology, Neurosurgical Service, College of Medicine, State University of Iowa.

1. Spiller, W. G.: The Occasional Clinical Resemblance Between Caries of the Vertebrae and Lumbothoracic Syringomyelia, and the Location Within the Spinal Cord of the Fibres for the Sensations of Pain and Temperature, Univ. Pennsylvania M. Bull. **18**:147-154, 1905.

2. Spiller, W. G., and Martin, E.: The Treatment of Persistent Pain of Organic Origin in the Lower Part of the Body by Division of the Anterolateral Column of the Spinal Cord, J. A. M. A. **58**:1489-1490 (May 18) 1912.

Foerster [3] has made sections at every cervical segment to and including the second and has obtained anesthesia in correspondingly high distributions. He has advised against bilateral cervical sections, however, at least at the same time, because of interference with respiration.

In order to eliminate pain in the upper extremity it is necessary to make a high cervical section and this has been done successfully. Peet, Kahn and Allen [4] reported a case of bilateral cervical chordotomy, one section being made at the third cervical and the other at the eighth cervical segment. The higher section eliminated pain in the contralateral arm.

Frazier and Spiller [5] reported a case in which section at the first thoracic segment resulted in involvement of the pupillary center.

Fay and Gotten [6] by using spinal anesthesia have given evidence to show that section made as low as the fifth thoracic segment may not abolish all pain in the lower extremity even though cutaneous pain may be lost. They suggested that some types of pain probably reach the cord at a higher level by way of the vessels and the sympathetic nerves. They found that a section above the third thoracic segment does abolish all types of pain. These findings may be of value in determining the site of election.

Motor Effects of Anterior Chordotomy.—Permanent motor impairment other than degrees of paralysis from injury to the pyramidal tracts has been uniformly absent. This is true of the cases in the literature as well as of our own cases. Despite the supposed function of the ventral spinocerebellar tract and the descending extrapyramidal tracts, no evidence of ataxia or incoordination has been elicited. One of our most striking cases was that of a patient with tabetic crises, in whom practically the entire anterior half of the cord was sectioned. That is, deep bilateral sections were made from the dentate ligaments to the anterior median fissure. There was flaccid paralysis for five days, and then progressive recovery to normal tone and motor function of the lower extremities within a month. No evidence of ataxia or incoordination

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3. (*a*) Foerster, O., and Gagel, O.: Die Vorderseitenstrangdurchschneidung beim Menschen, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:1-92, 1932. (*b*) Foerster, O.: Ueber die Vorderseitenstrangdurchschneidung, Arch. f. Psychiat. **81**:707-717, 1927.

4. Peet, M. M.; Kahn, E. A., and Allen, S. S.: Bilateral Cervical Chordotomy, for Relief of Pain in Chronic Infectious Arthritis, J. A. M. A. **100**:448-489 (Feb. 18) 1933.

5. Frazier, C. H., and Spiller, W. G.: Section of the Anterolateral Columns of the Spinal Cord (Chordotomy), Arch. Neurol. & Psychiat. **9**:1-21 (Jan.) 1923.

6. Fay, T., and Gotten, N.: Controlled Spinal Anesthesia: Value in Establishing Appropriate Levels for Chordotomy, Arch. Neurol. & Psychiat. **30**:1276-1281 (Dec.) 1933.

was observed. The patient was a carpenter and worked on scaffolding with a sure footing. It appears that in man the descending extrapyramidal tracts are not indispensable to normal tone and motor function.

Cadwalader and Sweet [7] found that ataxia and incoordination were marked in dogs after section of the anterolateral column and attributed the disturbances of function to section of the ventral spinocerebellar tracts and probably the rubrospinal and vestibulospinal tracts.

Sensory Effects of Anterior Chordotomy.—We believe that complete section of the spinothalamic tracts on one side at or above the third thoracic segment will abolish all pain and sense of temperature on the contralateral side from two or three segments below the section downward. This loss is permanent, and there has been no evidence of a bilateral representation of pain or temperature. In cases in which there appears to have been some return of "pain spots," the section has been incomplete.

If the section has not been made deep enough, the loss of pain sensibility will be greater during the first few postoperative days than subsequently.

If the section has been incomplete in an anterior-posterior direction the level of the loss of pain may retract toward the area of permanent loss a week or so after the operation. This appears to be true in regard to upper and lower levels in our cases of differential section (see case 6). That is, if some of the posterior fibers of the column are spared, the level of sensory impairment will subsequently retract upward; if some of the anterior fibers of the column are spared, the level will retract somewhat downward.

There has been equal impairment in discrimination of both pain and temperature in all of our cases. One has the impression that at the upper levels of sensory impairment one of these modalities may shade off more rapidly than the other, but interpretations are difficult. For example, one of our patients seemed to sense cold but not heat at the upper level of transition. The fact that discrimination of pain and discrimination of temperature have been segregated in cases of tumor of the cord is more probably due to differences in vulnerability than to differences in anatomic location of tracts mediating pain and temperature.

Frazier and Spiller [5] expressed the belief that fibers conducting pain and temperature do not ascend uncrossed and also that pain, heat

7. Cadwalader, W. B., and Sweet, J. E.: Experimental Work on the Function of the Anterolateral Column of the Spinal Cord, J. A. M. A. **58**:1490-1493 (May 18) 1912.

and cold are eliminated together, so that the fibers subserving these modalities must be mixed together.

So far as we know, Stookey [8] is the only one who has abolished the sense of pain without destroying the sense of temperature. He inserts the knife at the dentate ligament and brings it out just lateral to the anterior horn. He feels that the anterior spinothalamic tract probably conducts the sense of temperature, although his operation is the same as that performed by others.

It has been felt by many (including Head) that the tractus spinothalamicus ventralis mediates touch. Frazier and Spiller [9] could give no testimony to this, as their sections had not extended beyond the anterior horn.

One of us (O. H.) has made numerous deep sections extending to the anterior median fissure, and in no case were we able to elicit by the routine methods any loss in perception of light touch or of deep pressure, in two point discrimination or in the sense of position.

In none of our cases have we failed to eliminate pain. The series includes 3 cases of gastric crises, 2 of which are reported here (cases 2 and 5). The upper level of loss of pain reached the nipple line bilaterally in all 3 cases.

More striking than the prompt and permanent relief of demoralizing pain was the abolition, also permanent, of the vomiting or motor element of the crises.[10]

Oldberg [11] stated:

> There are certain things one must not expect this operation to do. One of them is to relieve the vomiting which is so often associated with gastric crises of tabes dorsalis. This vomiting is vagal in character and so, of course, would not be affected by a spinal cord operation.

Although this would naturally be one's first impression, the facts are fortunately more favorable.

Kahn and Barney [12] reported an interesting case in which bilateral chordotomy was done at the fifth thoracic segment in a patient suffering from gastric crises. The level of loss of pain was at the umbilicus, and the crises were not relieved. The splanchnic nerves were sectioned, and

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8. Stookey, B.: Human Chordotomy to Abolish Pain Sense Without Destroying Temperature Sense, J. Nerv. & Ment. Dis. **69**:552-557 (May) 1929.

9. Spiller, W. G., in discussion on Frazier, C. H.: Section of the Anterolateral Columns of the Spinal Cord for the Relief of Pain: Report of Six Cases, Arch. Neurol. & Psychiat. **4**:575-576 (Nov.) 1920.

10. Case 5 is a possible exception.

11. Oldberg, E.: Chordotomy for Relief of Pain, S. Clin. North America **12**: 1315-1322 (Oct.) 1932.

12. Kahn, E. A., and Barney, B. F.: Anterolateral Chordotomy for Intractable Pain of Tabes Dorsalis, Arch. Neurol. & Psychiat. **38**:467-472 (Sept.) 1937.

later the rami communicantes of the eleventh and the twelfth thoracic nerves. The pain being still unrelieved, bilateral chordotomy was done at the seventh cervical segment, and this was followed by complete relief.

Our conclusion is that gastric crises (both pain and motor elements) can be eliminated, but a bilateral section must be made at or above the third thoracic segment, so as to include the chest in the region of analgesia.

Other Factors.—Retention of urine necessitating catheterization for ten to fourteen days has occurred in our cases after complete bilateral section beginning at the dentate ligament. Retention has not occurred after unilateral section. This has been the experience of Sicard and Robineau.[13] In case 6, in which minimal differential bilateral section was done, postoperative retention of urine lasted only two days, even though the patient had shown impairment of vesical tone preoperatively. We feel that this unpleasant sequel of bilateral section will be greatly obviated if complete section of the pain tract is performed with minimal destruction of the cord, as is subsequently suggested.

Patients cannot distinguish wetness in involved zones. They distinguish hair pulling, but without pain. The sensation of tickling was lost on the soles in 2 patients and was retained in others. The subjective sensation in the lower extremities has invariably been one of warmth and comfort.

Bilateral section destroys in the male the ability to have sexual intercourse and orgasms, though it does not always destroy sexual desire. Erection was impossible in one patient. One woman reported that the voluptuous sensation of intercourse was lost. No patient so far has regretted the operation because of this sequela.

One of the most intriguing facts related to chordotomy is that the patient feels no pain when the spinothalamic tract is cut, nor has a patient ever complained of referred pain in the distribution of the severed tract comparable to that occurring after section of a nerve root. Feeling that impulses of pain must be combined with those of touch in order to be properly interpreted, one of us (O. H.) had his assistant stroke the posterior columns while the "pain tract" was being cut. Although the patient felt a constricting pressure about the groins, he denied that there was pain. This is another evidence that artificially provoked impulses in neurons of the second order have an unexpected and entirely different physiologic result from such impulses in neurons of the first order.

Girdle pain commonly follows chordotomy and is proportional to the degree to which the posterior roots have been manipulated. It is some-

13. Sicard and Robineau: Cordotomie latérale antérieure pour algies incurables, Rev. neurol. **1**:21-28 (Jan.) 1925.

times troublesome for a long period if filaments of a posterior root were unwittingly crushed when the dentate ligament was grasped. Great care should be exercised in dissecting the dentate ligament free from both posterior and anterior root filaments. Should a posterior root be injured it is preferable to sever it entirely.

In a case of medulloblastoma with metastases to the cord the anterior spinal artery was accidentally cut. Complete paralysis ensued, which we feel was attributable to ischemia.

TOPOGRAPHIC ANATOMY OF THE CORD

It appears that insufficient attention has been given to the precise location of the dentate ligaments and the line of entry of the anterior roots as the operator sees them.

It has usually been implied that the coronal plane of the dentate ligaments equally divides the cord. In a study of several cords we observed that this plane more nearly passes through the junction of the posterior third of the cord with the anterior two thirds.

The line of entry of the anterior roots does not correspond with the position of the anterior horns as it is often represented to do but is situated lateral to the horns. The line formed as the anterior roots enter the cord is definite and is slightly more than half the distance from the dentate ligament to the anterior median fissure.

We have prepared the diagrams which accompany the case reports to represent a close reproduction of the topography of the cord. The statements made here and the diagrams, of course, have reference to the thoracic portion of the cord at the level of the third dorsal vertebra.

TECHNIC

In the cases to follow, all sections of the cord were made beneath the second or the third dorsal laminal arch. When bilateral sections were made, they were separated by ½ to 1 inch (1.2 to 2.5 cm.). Posterior roots were sectioned only in cases in which it is specifically stated that they were. All operations were done with the region under local anesthesia (2 per cent procaine hydrochloride in the skin and 0.5 per cent procaine hydrochloride in the muscles to the transverse processes). The initial infiltration was sufficient. None of the patients complained of pain when bone was removed or during any part of the operation except when direct manipulation or pinching of a posterior root occurred. They were cooperative during the sensory tests. Some of these were made by one of us (C. Van E.) and some by Dr. J. W. Dulin.

The sections were made with a narrow-bladed cataract knife.

REPORT OF CASES

CASE 1.—D. C., a white man aged 38, entered the hospital on March 5, 1938, complaining of severe and constant pain in the left hip and leg. In August 1937 a disarticulation of the right humerus had been done for osteochondrosarcoma. On admission to the hospital on March 5 there was roentgen evidence of metastases in the chest and in the fourth lumbar vertebra.

Chordotomy was done as indicated in figure 1. The patient was comfortable and free from pain at the time he left the hospital, four weeks later.

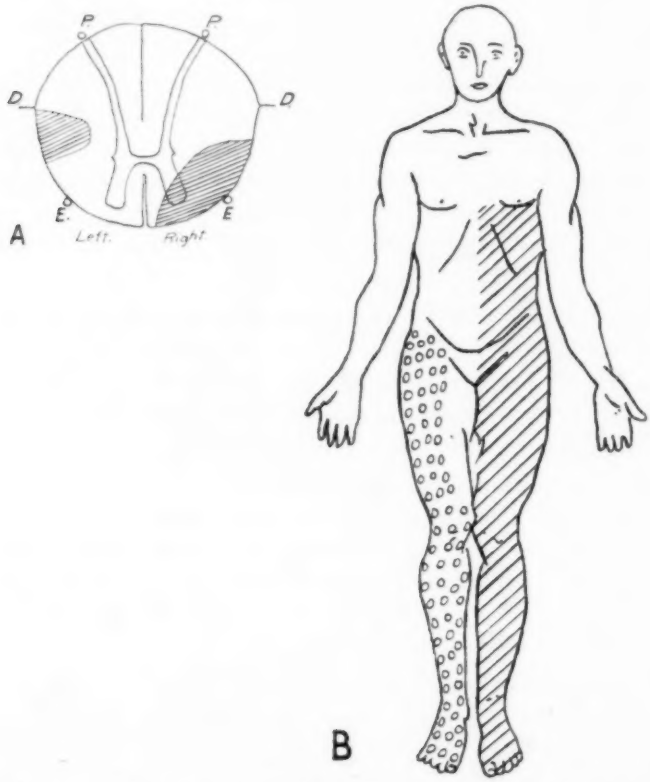

Fig. 1 (case 1).—*A*, diagram indicating the manner in which the cord was sectioned. *P*, line of entry of the posterior roots; *D*, dentate ligament; *E*, line of entry of the anterior roots. *B*, drawing to show the results of the sections. The cross hatching indicates complete loss of pain and of temperature sense. The circles indicate partial loss in these modalities. There appeared to be areas roughly 0.5 cm. in diameter which would be normally sensitive to pain, whereas in an adjacent similar area pain was lost.

CASE 2.—L. K., a white man aged 56, entered the hospital in March 1938 because of gastric crises. He had contracted syphilis in 1913, and for three and one-half years prior to his admission to the hospital he had gastric crises (abdominal pain and vomiting) progressing in severity.

Antisyphilitic therapy produced negativity of the Wassermann reaction, and there was relatively little evidence of damage to the posterior columns of the spinal cord. The gastric crises, occurring several times a week, were severe, and for three months he had had continuous pain girdling the chest.

Chordotomy was done as indicated in figure 2. The patient voided urine voluntarily from the first day after the operation. He has remained free from crises (both pain and vomiting) to the present writing (six months).

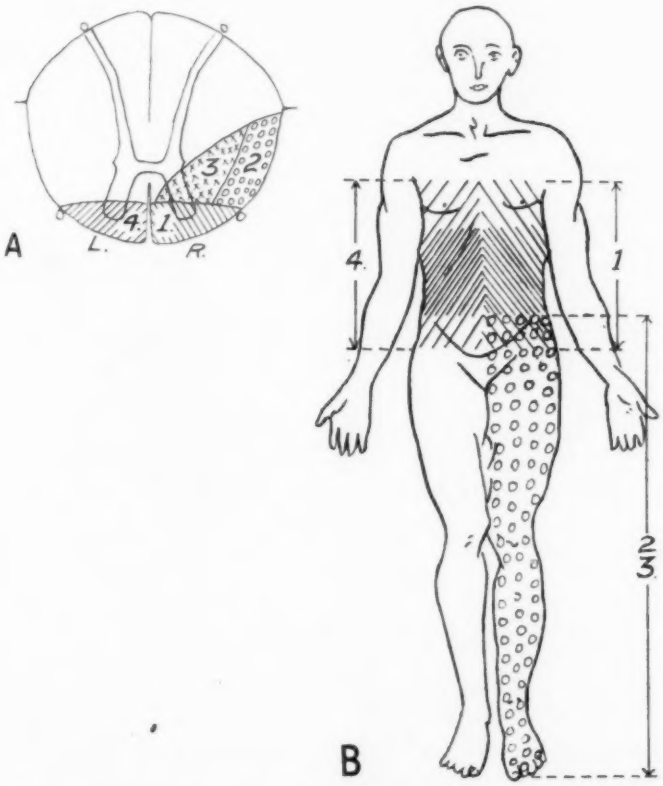

Fig. 2 (case 2).—*A*, diagram indicating the manner in which the sections were made. The numbers indicate the order in which the sections were made. *B*, drawing to show the results of the sections. The close hatching indicates complete loss of pain and of temperature sense. The wide hatching indicates about 50 per cent loss in these modalities. The circles indicate complete loss in both modalities, but this was not fully obtained until section 3 was made.

Case 3.—J. H., a white man aged 67, entered the hospital on July 11, 1938, complaining of severe postherpetic neuralgia in the distribution of the eighth, ninth and tenth thoracic nerves on the left. He had had herpes zoster in January.

Unilateral chordotomy was done as indicated in figure 3. Complete relief was obtained. For technical reasons, the third dorsal posterior root was sectioned on

each side. This produced an indefinite sensory loss on the right side of the chest, which is not indicated in the diagram.

There was no difficulty in voiding urine at any time after the operation.

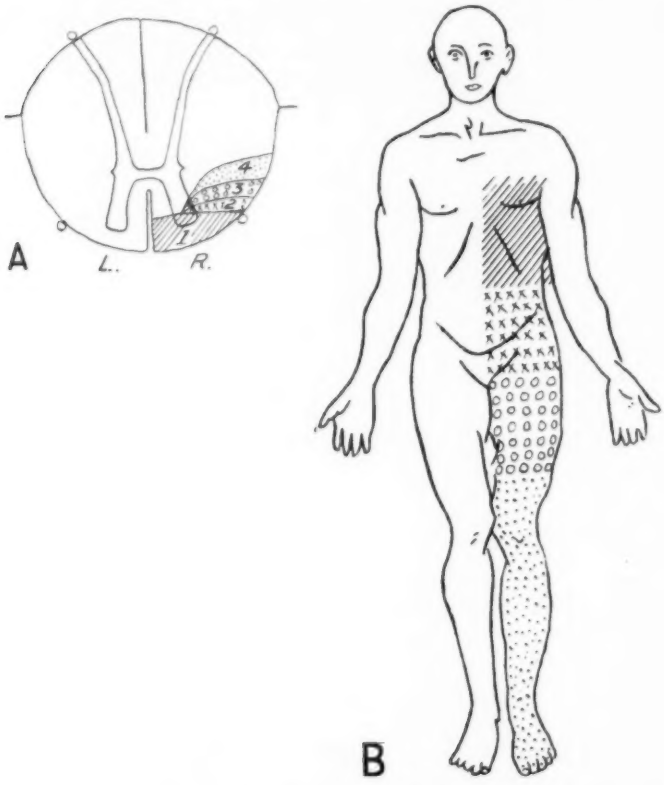

Fig. 3 (case 3).—*A*, diagram indicating the manner in which sections were made. *B*, drawing to indicate that a final complete loss of pain and of temperature sense reached a level at about the nipple line. Note that the level in this case was caused to progress downward, the reverse of that in the following cases. After section 1 the patient stated that he no longer felt the old pain, and the skin, which had been scarred by herpes, could now be rubbed without discomfort. This section, which caused a loss of pain and of temperature sense limited to the left side of the chest, would probably have been sufficient.

Case 4.—H. S., a white man aged 24, entered the hospital April 14, 1938, complaining of relentless pain in the back and thighs. In May 1936 an abdominoperineal resection of the rectum had been done because of carcinoma. Metastases were evident in the inguinal nodes and the bladder when he entered the hospital in 1938.

Morphine afforded little relief, and chordotomy was performed. The sections were made as indicated in figure 4.

Inasmuch as control of the bladder had been lost for some time, return of vesical function was not expected.

The patient was comfortable and entirely free from pain until his death on the sixteenth postoperative day.

The results of studies on the cord are shown in figure 5.

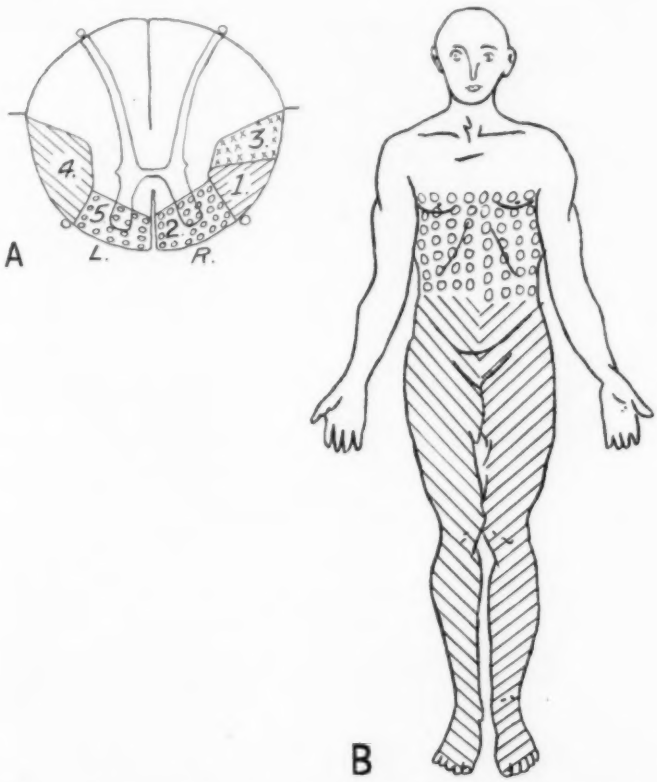

Fig. 4 (case 4).—*A*, diagram indicating the manner in which the sections were made. The numbers indicate their order. *B*, circles and hatching indicating complete loss of pain and of temperature sense. Note that sections 1 and 4 produce about the same upper level; section 3 had no additional effect, and sections 2 and 5 raised the level to the nipple line.

CASE 5.—C. K., a white man aged 27, entered the hospital in April 1938, complaining that he had suffered from attacks of abdominal pain and vomiting for three years. The attacks of vomiting began first, the painful element being superimposed later. At least one attack occurred each week and was typical of a gastric crisis except that the vomiting seemed more severe than the pain. Extensive antisyphilitic therapy had been given, but the Wassermann reaction was positive. There was only mild damage to the posterior columns, as demonstrated by clinical tests.

Chordotomy was carried out as indicated in figure 6.

The patient began to void urine normally by the fifteenth postoperative day.

To the present time, four months after the operation, he has had no pain and has vomited only twice.

CASE 6.—P. Z., a man aged 64, entered the hospital on April 25, 1938, with a complaint of pain in the abdomen and in the back. A supraclavicular node con-

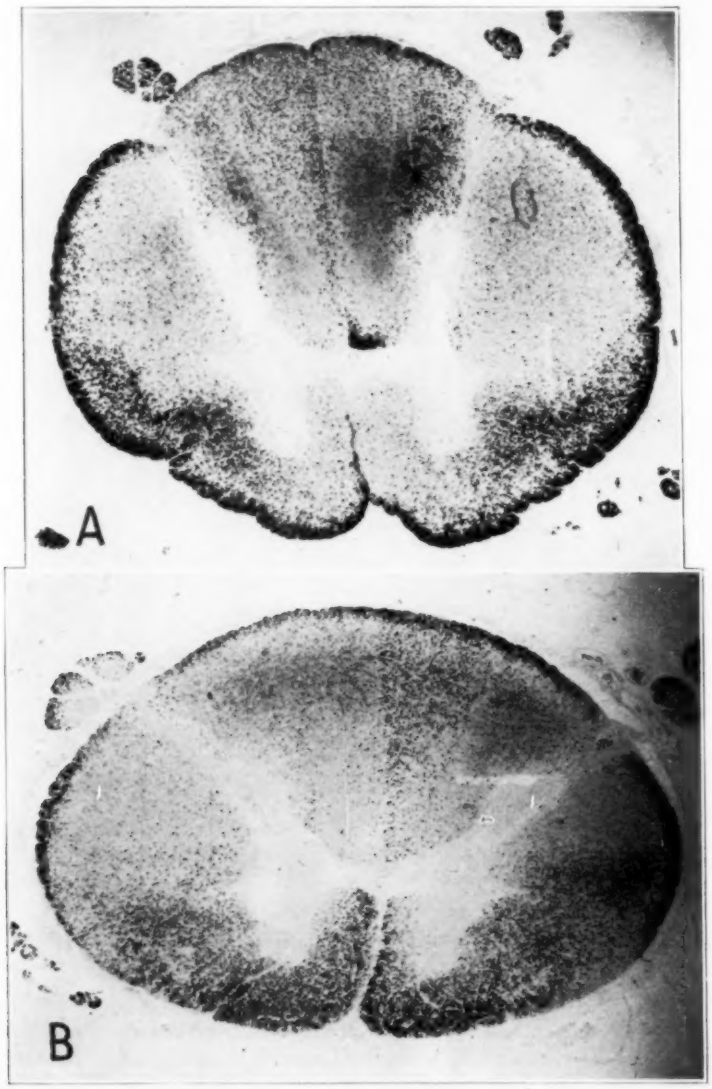

Fig. 5 (case 4).—*A*, Marchi preparation showing degeneration of the ascending fibers at the first thoracic level. (See figure 10 *E*, which is a diagrammatic tracing of this photograph.) *B*, Marchi preparation showing degeneration of the descending fibers at about the level of the fifth thoracic segment.

tained an adenocarcinoma, and a provisional diagnosis of carcinoma of the pancreas with diffuse abdominal metastases was made. Pain in the back, epigastrium and abdomen became so acute that the patient eagerly consented to chordotomy.

When the sections were made as indicated in the diagram (fig. 7) the patient stated that his pain had disappeared. Sensory tests substantiated his statement, and no further sections were made. The operation appeared to be no ordeal, and the patient was most grateful for complete relief from pain during his last days.

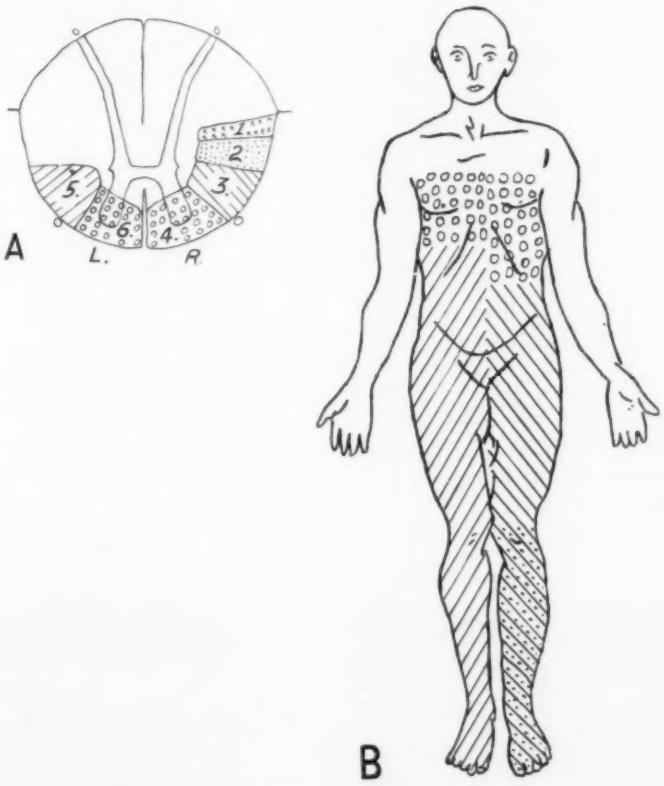

Fig. 6 (case 5).—*A*, diagram indicating the manner in which the sections were made. *B*, drawing to indicate the final complete loss of pain and of temperature sense, reaching a level at the nipple line. Section 1 made no detectable changes. Section 2 resulted in a spotty (50 per cent) loss of pain from the left knee down.

Vomiting, which had been persistent for two weeks, continued as before. Although he had had moderate difficulty in voiding urine before the chordotomy, this function was restored on the third postoperative day. He clearly perceived fulness of the bladder and desire to void.

He died on the twelfth postoperative day, and the results of a study of the cord are shown in figures 8 and 9.

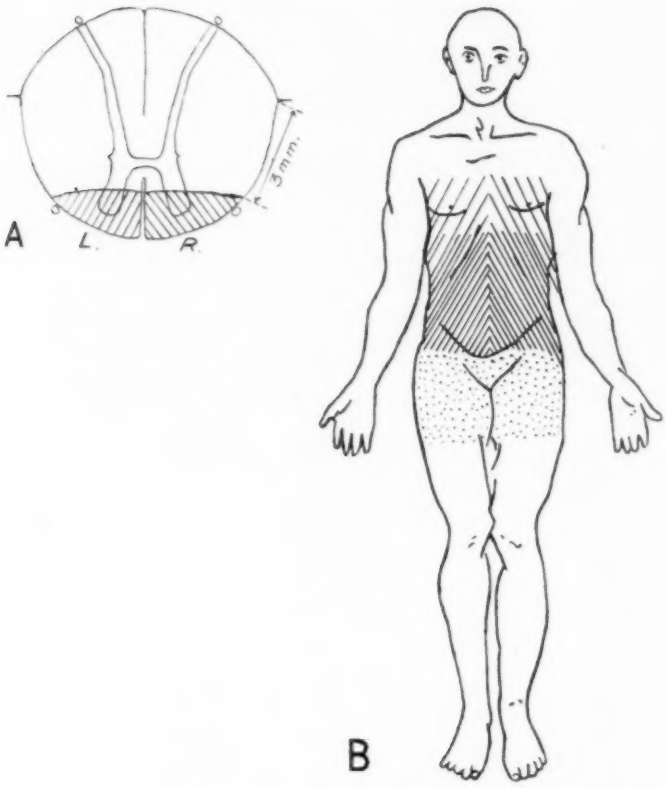

Fig. 7 (case 6).—*A*, diagram indicating the manner in which the cord was sectioned. *B*, drawing to show the results of the sections. The close hatching indicates loss of pain and of temperature sense, shading off above at the area of wide hatching and below at the stippled region. The loss of pain was complete in the stippled region on the day of operation, but this level retracted by the third postoperative day.

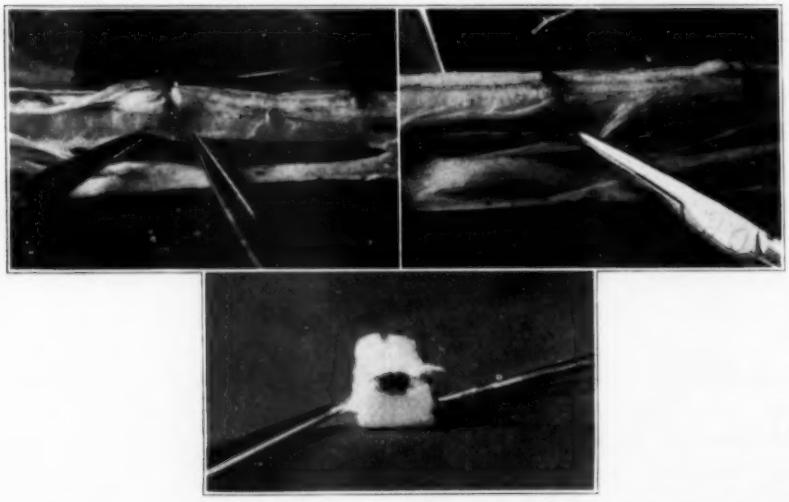

Fig. 8 (case 6).—Photographs showing the sections at different levels and a cross section of the cord through the lower section. In making each section the knife was inadvertently carried across the anterior median fissure but fortunately without cutting the anterior spinal artery. Hemostats are shown grasping the dentate ligaments in each case, and the distance from the ligament to the section can be clearly seen.

COMMENT

Optimum Location and Extent of Section.—So far as we know, all surgeons have begun their sections just anterior and close to the attach-

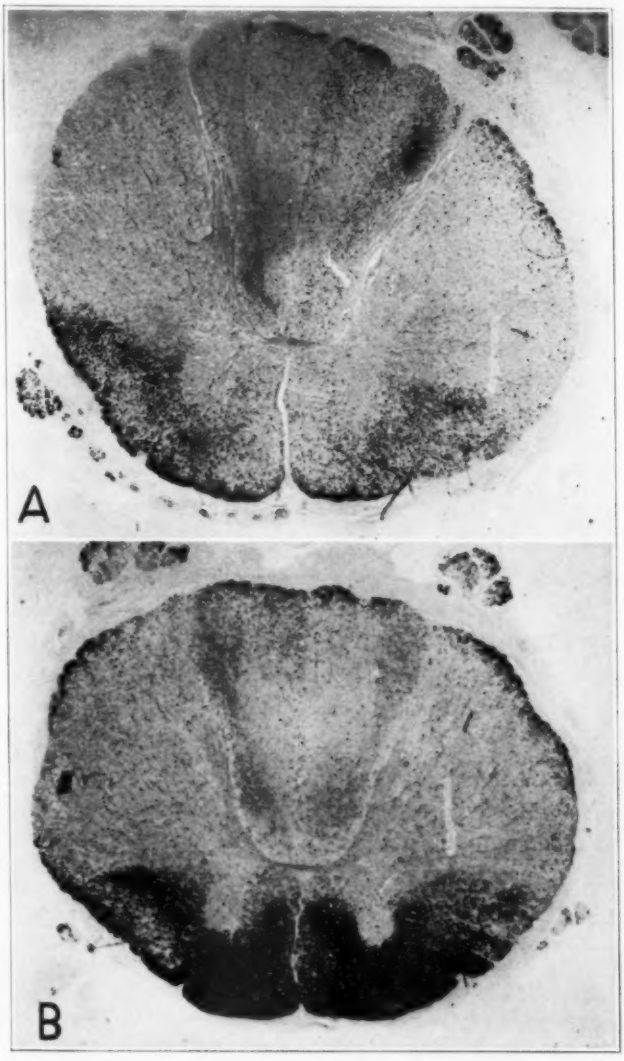

Fig. 9 (case 6).—*A,* Marchi preparation showing degeneration of the ascending fibers at the level of the first thoracic segment. Some of the posterior fibers have been spared. Compare with figure 5 *A*. *B,* Marchi preparation showing degeneration of the descending fibers between the levels of the fourth and fifth thoracic segments.

ment of the dentate ligament. According to the earlier literature the section was carried to or not quite to the anterior roots. However,

as more cases were studied, certain authors recognized that better results were obtained if more of the cord was included anteriorly. Peet [14] gained the impression that levels of sensory loss were higher if the incision was carried through, and not merely to, the anterior root.

Kahn and Barney [12] felt that the section should be carried 2 mm. beyond the anterior root.

Frazier [15] in 1of a series of 6 bilateral chordotomies failed to obtain a sensory loss on one side.

Horrax' cases [16] indicate that his sections were not carried far enough anteriorly when the chordotomy was at a high thoracic level and high levels of sensory loss were desired. His routine section appeared sufficient when carried out at or below the level of the eighth thoracic segment. His cases also suggest that partial losses in an involved zone are due to failure to make the sections deep enough.

Sections carried to the anterior root may prove to be complete when done at low thoracic levels. As to this we are not prepared to make a statement at present, although our Marchi preparations indicate that the spinothalamic tract extends farther forward than the anterior root —at least as low as the fifth thoracic segment. Foerster's [3] preparations indicate that the fasciculus migrates posteriorly as the upper cervical segments are transgressed.

Leighton [17] made his incisions 2.5 mm. deep and 3 mm. wide, beginning at the dentate ligament and ending just behind the anterior roots. The sections were made under the fifth, sixth and seventh thoracic laminal arches, and the levels of sensory loss, when mentioned, were said to be about six segments lower. He endorsed the advice of Spiller that the section might with advantage be carried forward to include the anterior root.

The first chordotomy reported [2] is also interesting in this respect. Martin, who did the operation, stated:

> The problem presented by Dr. Spiller was the making of a transverse cut into the spinal cord, roughly 2 mm. in length, of a similar depth, and with its posterior end 3 mm. anterior to the entrance of the posterior root, this cut to be bilateral.

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14. Peet, M. M.: The Control of Intractable Pain in Lumbar Region, Pelvis and Lower Extremities by Section of the Anterolateral Columns of the Spinal Cord (Chordotomy), Arch. Surg. **13**:153-204 (Aug.) 1926.

15. Frazier, C. H.: Section of the Anterolateral Columns of the Spinal Cord for the Relief of Pain: Report of Six Cases, Arch. Neurol. & Psychiat. **4**:137-148 (Aug.) 1920.

16. Horrax, G.: Experiences with Chordotomy, Arch. Surg. **18**:1140-1164 (April) 1929.

17. Leighton, W. E.: Section of the Anterolateral Tract of the Cord for the Relief of Intractable Pain Due to Spinal Cord Lesions, Surg., Gynec. & Obst. **33**:246-249 (Sept.) 1921.

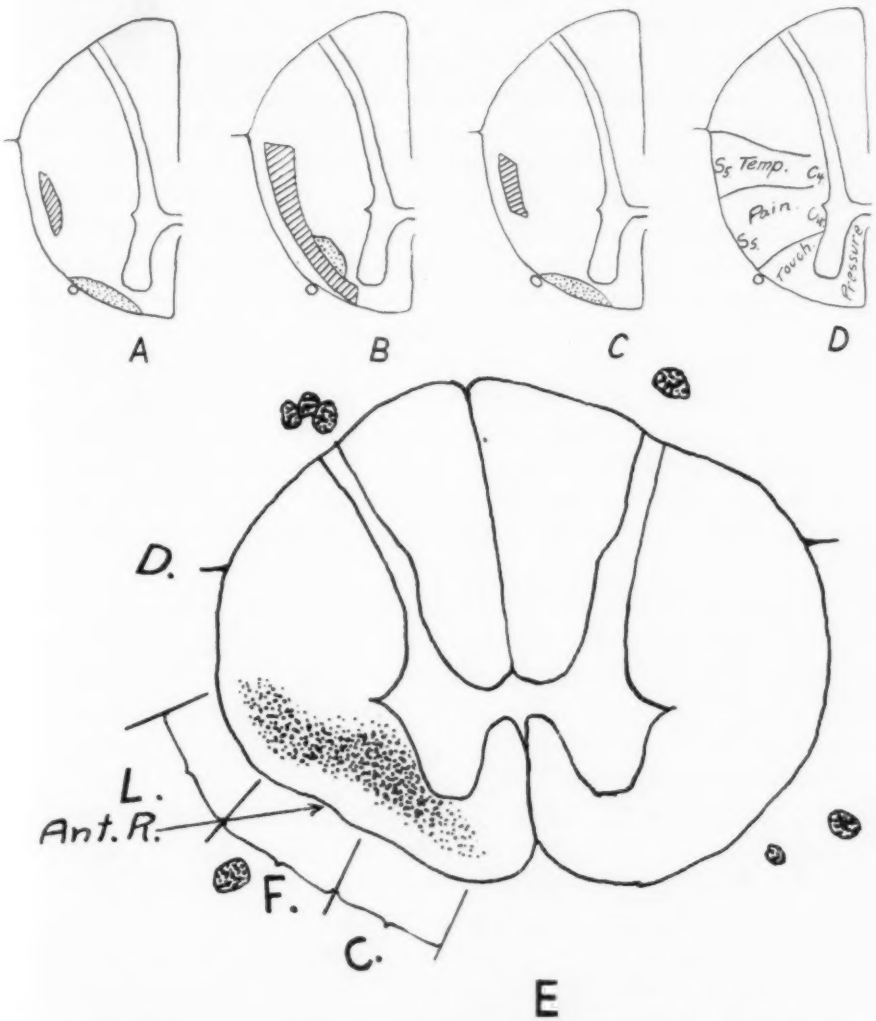

Fig. 10.—Diagrammatic representations of the spinothalamic tracts as given by several authors. *A*, drawing taken from Gray (Gray, H.: Anatomy of the Human Body, ed. 20, edited by W. H. Lewis, Philadelphia, Lea & Febiger, 1918, p. 759). *B*, drawing taken from Tilney and Riley (Tilney, F., and Riley, H. A.: The Form and Functions of the Central Nervous System, New York, Paul B. Hoeber, 1923, p. 196). *C*, drawing taken from Ranson (Ranson, S. W.: The Anatomy of the Nervous System, Philadelphia, W. B. Saunders Company, 1920, p. 110). *D*, drawing taken from Foerster.[3] *E*, our own concept of the tract, made from a tracing of figure 4 *A*.

L, fibers probably representing the lower extremity; *F*, fibers representing the groin and abdomen; *C*, fibers representing the chest; *D*, dentate ligament; *Ant. R*, line of anterior roots.

Spiller stated that objective sensation was lost in the anterior surfaces of the thighs but that pain and pinprick sensations were keen over the lower portion of the abdomen.

From a study of our cases we feel that the spinothalamic tract in the high thoracic region extends from a coronal plane about two-fifths the distance from the dentate ligament to the anterior roots to a sagittal plane about three-fifths the distance from the anterior root to the anterior median fissure (fig. 10 *E*). The tract broadens out in the region lateral to the anterior horn so that it hugs close to the latter structure and well fills the area between the anterior and the lateral horn. The minimal section, to include all the fibers of the spinothalamic tract should begin about 2 mm. anterior to the dentate ligament and emerge 2 to 3 mm. mesial to the anterior roots. The section should extend deep enough to skirt the lateral and anterior horns, 3 mm. of actual depth being sufficient. Patients in whom sections have been made in this manner have given clinical evidence of complete section of the tracts mediating pain and temperature. The 2 mm. region adjacent to the dentate ligament we feel contains no fibers conducting sensations of pain or temperature.

Disposition of Fibers Conducting Pain.—Foerster [3] has proposed that the fibers are arranged in a laminated fashion—those from the lowermost segments of the body occupying a place at the periphery of the tract and those of the higher segments disposing themselves toward the center of the cord (fig. 10 *D*). This concept appears to have been generally accepted.

Our studies indicate that fibers representing the lower segments are situated posteriorly in the tract and fibers representing successive segments upward dispose themselves more and more anteriorly (fig. 10 *E*).

Hence it has been possible to eliminate pain in the chest and abdomen without including the lower extremities. These results should point to more favorable results from chordotomy inasmuch as the section is removed from the region of the pyramidal tracts by a greater and safer distance than heretofore. Less extensive incisions are followed by lower morbidity and fewer sequelae. The differential section may prove of value in eliminating pain in the upper extremity, though we have not had such a case as yet.

CONCLUSIONS

1. The spinothalamic tract mediating the sensations of pain and temperature extends from a point about midway from the dentate ligament to the anterior roots to a point about midway from the anterior roots to the anterior median fissure. Hence a complete section should

include this region. The region extending 2 mm. anterior to the dentate ligament contains no fibers conducting sensations of pain or temperature (fig. 10*E*).

2. As one progresses from the lower segments of the body upward, the corresponding "pain fibers" are disposed more and more anteriorly in the cord.

3. It is possible, therefore, by differential section to eliminate the sensations of pain and temperature in the chest and to retain these modalities in the lower extremities.

FUNCTIONAL CAPACITY OF THE UNDESCENDED TESTIS

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MINNEAPOLIS

I. GENERAL CONSIDERATIONS

The purpose of this paper is to present a study of the functional capacity of the undescended testis, with special reference to its potentialities for the production of spermatozoa.

While much has been written about the histologic character of the undescended testis, little attention has been paid to its function. Nearly all physicians agree that the anatomic results of surgical treatment are good, but few have inquired about the function of the organs after their placement in the scrotum. The facts recently established by research workers and clinicians in this field of endocrinology are especially significant, though as yet they are incomplete. Important discoveries are constantly clarifying physicians' views and permitting definite therapeutic advances.

The histologic aspects and the treatment of the undescended testis have been thoroughly discussed by Moore, Wangensteen, Meyer, Bevan, Cabot, Coley and others. However, a review of these subjects is given in order that there may be a better understanding of the clinical and experimental results to follow.

1. *Incidence.*—Undescended testes occur in from 0.1 per cent (Marshall) to 0.12 per cent (Monod and Terrillon) of males. Statistics on the Austrian army show that the incidence of undescended testes in every 1,000 men drafted for military service (Ziebert) was 2.2. According to the medical records of the United States War Department for the World War, there were 3.1 cases of ectopy for every 1,000 men examined. Eccles found undescended testes in 2 per cent of 48,000 cases of hernia. Bevan, Coley and Wangensteen put the incidence of retained gonad at 1 in 500.

Incomplete descent is more common on the right than on the left side. From the statistics of Berger, Hofstätter and others, the incidence of maldescent of the right testicle is equal to that of bilateral maldescent

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Abridged from parts of a thesis submitted to the Graduate Faculty of the University of Minnesota in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Surgery, in May 1937.

and retention of the left testicle combined. In 20 per cent of cases of undescended testes the deformity is bilateral (Wangensteen).

2. *Causes.*—The causes of nondescent of the testis are unknown. Factors said to bring about retention of the gonad have been classified by Eccles as abnormalities of the mesorchium, of the testis and its component parts, of the gubernaculum, of the cremaster, or of the route along which the testis must pass. To these causative factors probably should be added endocrine imbalance.

McGregor concluded that ectopy of the testis can be explained on anatomic grounds. He stated that one or more of the following congenital factors are present: (1) anomaly or absence of what he called the "third inguinal ring," (2) fascial pockets and (3) fascial ridges. His careful dissections well explain the four varieties of retained testes, namely, the inguinal, the pubopenile, the perineal and the crural or femoral. Like most contemporary authors, he has questioned the gubernacular theory of descent. His own studies failed to demonstrate any subdivision of the gubernaculum, nor did they determine what causes descent.

3. *Histologic Appearances.*—Hunter concluded that the undescended testis fails to reach the scrotum because of its inherent imperfection. This cannot be wholly true, at least from an anatomic point of view, because it is impossible to distinguish histologically between a normal and a retained testis if the subject is below the age of puberty.

The histologic aspects of the retained gonad have been reviewed by a number of investigators (Eccles; Felizet and Branca; Rawling; Moore; Southam and Cooper; Pace, Wangensteen and others). Wangensteen summarized the observations as follows: The normal testis grows but slightly from birth to puberty, during which time there are few histologic changes. The undescended testis before puberty resembles the scrotal gland in weight and minute anatomic structure (table 1). With the onset of puberty, however, the normal testis shows a sharp increase in weight, which is due to the elaboration of mature epithelium and to the appearance of spermatozoa. The undescended testis exhibits these changes to a lesser degree. Wangensteen had never seen spermatozoa in the seminiferous tubules of a testis retained after puberty. This agrees with the observations of Felizet and Branca, who found that while a few undescended testes contained spermatogonia and spermatocytes, only 2 of 51 contained spermatids and none contained spermatozoa.

Southam and Cooper concluded that the farther the preadolescent testis has descended the more closely it corresponds to the normally located gland of the same age. However, a large series of cases would be necessary to verify this statement. Certainly the histologic picture of an abdominal gonad is often indistinguishable from that of an inguinal

TABLE 1.—*Gross and Microscopic Anatomy of the Descended and Undescended Testis*

Anatomy	Normal Descended Adult Testis	Undescended Adult Testis	Normal Descended Testis of Newborn	Normal Prepubertal Testis	Undescended Pubertal Testis
Macroscopic	Ovoid shape; wt., 25 Gm. each; digital fossa usually closed but may be open	Preserves contour, but smaller in proportion; body and tail may be separated from testis by mesorchium	Ovoid or bean shape; wt., 0.5 Gm.	At 15 years, wt., 11-12 Gm.; tunica albuginea and Highmore body become thicker	"Primary atrophy" (Felizet and Branca); "underdeveloped testis" (Kyrle); separation of epididymis and testis by a digital fossa; thicker tunica albuginea and Highmore body
Microscopic					
Seminiferous tubules	1. Several layers of epithelium	1. Germinal epithelium disappears 2. Outline of tubule may persist as hyaline ring	1. Diameter of tubules, 60 microns 2. No real lumens 3. 2-3 rows of irregular cells fill tubules	Diameter of lumen, 85-90 microns	1. Diminution in size of tubules 2. Isolation of tubule 3. Lined by epithelial cells, as normal descended testis
(a) Sertoli cells	1. Lie on basement membrane of tubules 2. Nuclei rich in chromatin 3. High fat content in cytoplasm	1. Only a single layer of epithelium consisting of Sertoli cells, may be present	1. Sertoli cells more frequent in proportion to spermatogonia	1. Definite arrangement of Sertoli cells 2. Sertoli cells less frequent in proportion to spermatogonia	1. After puberty undergoes degenerative change 2. More differentiated at 10 years
(b) Spermatogonia	1. Scattered among Sertoli cells 2. Nuclei rich in chromatin; spermatocytes I° → spermatocytes II° → spermatids → spermatozoa	1. Absent unless just past puberty or persistence in quiescent state of nuclei of spermatogonia	1. Present singly or in groups, 1 spermatogonium to 35-40 Sertoli cells	1. Increase in number of spermatogonia, 7:20 Sertoli cells 2. Adult germinal cells become differentiated	1. Present; early, in repose later (see mitosis and spermatocytes); even spermatozoa, especially in early postpubertal period
Intertubular spaces	1. Loose	1. Increase in stroma causes tubules to be more widely separated	Delicate CT between tubules	CT between tubules contains elastic tissue	Increase of interstitial tissue, which appears in form of embryonic nucleated stroma
(a) Interstitium and (b) Interstitial cells	a. Small eccentric nuclei B. Finely granular cytoplasm c. Crystallized bodies in cytoplasm	1. Apparent but not real increase of interstitial cells	Not so prominent in fetal life	.....	1. Interstitial cells are in abeyance till 10 yr. as in prepubertal descended testis

testis. The time factor is probably as important as the degree of descent in determining the histologic picture, barring any congenital malformation.

4. *Malignant Tumor of the Undescended Testis.*—Pain, torsion, hernia and malignant tumor are the most common complications of testicular maldescent. There has been much discussion about the incidence of malignant tumor of the undescended testis. Hinman reviewed 649 cases of cancer of the gonads and found undescended testes involved in 12.2 per cent. Coley, Cunningham, Odiorne and Simmons, Schischko, Lipschütz and Dean altogether reported 1,371 cases of malignant change in the male sex gland. The undescended organ was the site of malignant growth in 136, or 9.9 per cent. Since only from 0.12 to 0.2 per cent of testes are undescended, the ectopic testis appears to be involved fifty times more often than its incidence would justify. Rubaschow reviewed the cases of undescended testis reported by 21 observers and found that in 11 per cent of the whole group tumors were present, a figure in striking contrast to the 0.05 to 0.06 per cent incidence of neoplasm in the testis (Rea).

It is evident that the ectopic testis is definitely more liable to neoplasia than is the normal gland. However, the actual percentage of undescended testes undergoing malignant degeneration is another question and is the phase most commonly overlooked in the discussion of this subject. Eccles observed 859 cases of undescended testis without finding malignant tumor. Coley did not have a single case of malignant tumor in 1,357 cases of undescended testes. Kocher found only 1 case of neoplasm in 1,000 cases of maldescent. Up to 1931, MacKenzie and Ratner had never observed an instance of malignant tumor in a series of 105 cases of undescended testis. However, in 1934 they reported 3 cases in which malignant tumor occurred in retained glands. Pace found adenocarcinoma in 3 of 24 undescended testes. It should be stated, however, that the series was small, that in 1 case the diagnosis was questionable and that the degrees of malignancy were low (grade 1). Hinman stated that 3 of 155 cryptorchids had a testicular tumor—about 1 in every 50, or 2 per cent. If one checks the records of the Division of Vital Statistics at Washington, D. C., one finds that possibly 3.2 per cent of undescended testes become malignant.[1]

1. In the registration area in 1935 there were about 1,400,000 deaths. Assuming that half of those who died were males (700,000) and considering the fact that 1 in 500 males had undescended testes, I conclude that about 1,400 men with undescended testes died in 1935. In the same year 458 men died of malignant tumor of the testis. Since malignant tumor occurs fifty times more frequently in undescended than in descended testes, $50 : 500 = x : 458$, in which x equals the number of men who died of malignant tumor of the undescended testis. Therefore, $x = 45.8$. If 45.8 of 1,400 cryptorchids died with malignant tumor of the testis, the incidence of this condition in cryptorchids was 3.2 per cent.

Haberland claimed that 0.75 per cent of undescended testes in animals eventually show malignant tumor. Clinically the incidence of malignant change in retained testes does not seem to be higher than that in normal breasts or uteri (2 per cent). This is a contradiction of the indiscriminate castration of cryptorchids for fear of malignant change.

When one considers the low incidence of malignant degeneration in undescended testes, as well as the fact that in 20 per cent of cases of retained testes the condition is bilateral and the generally poor results in the treatment of testicular neoplasms, one must conclude that the procedure of choice in the treatment of the ectopic gland is orchiopexy. That orchiopexy per se does not protect against malignant developments has been mentioned in the reviews of Wangensteen and Rea, as there are instances in which malignant tumor later occurred in testes on which the operation had been done. However, this and the other evidence cited would tend to show that it is not so much the position as "the biophysical and chemical factors involved in the growth of tissue" that plays the important role in neoplasia of the undescended gland (Hinman).[2]

5. *Internal Secretion of the Retained Testis.*—The existence of a male sex hormone, androgen, has been recognized for a long time. The interstitial cells, first described by Leydig in 850, were regarded as its source by Bouin and Ancel in 1903. The hormone is thought by most investigators to be unrelated to spermatogenesis. However, since some germinal epithelium usually persists in most conditions of aspermia, as in undescended or irradiated testis, Oslund stated that it has not been determined whether the germinal epithelium, the interstitial cells or both produce the hormone. Some workers have regarded the interstitial cells as secretory, while others have concluded that they are no more than modified connective tissue cells (Moore).

The effects of deprivation of this hormone, as by castration, are well known. As the effects of its removal are immediate, none of the substance appears to be stored in the body. Deficiency during the development of the organism will affect the accessory and secondary organs of sex; deficiency after development will affect their normal activity (Moore). The effect of castration on the epididymis, the vas deferens, the seminal vesicle and the prostate is so constant that Moore has used it as a "testis-hormone indicator." The high columnar epithelium of the seminal vesicle of the rat changes considerably within twenty days after castration. The subcutaneous injection of the purified lipoid extract of fresh bull testis restores the vesicle of a castrated rat.

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2. Most of the foregoing data and statistics are mere rationalizations, however. The whole problem will be settled only by more records of the number of patients with undescended testes dying of a malignant neoplasm of the testis.

Guinea pigs within three months after castration lose the reflex of ejaculation on electrical stimulation of the brain, but it reappears within two weeks after the subcutaneous injection of fat-soluble androgenic substance. Capons have also been used in tests for the presence of androgen; in fact, the first testicular graft, by Berthold (1849), was of this type. If androgen is present, castrated chickens, even females, will grow combs, wattles and ear lobes. The urine of normal men contains a substance which promotes growth of combs in capons (see reviews of Moore, Koch and Hinman).

It has been proved by the capon comb test that androgen is present in cases of single and bilateral testicular maldescent (Koch; Webster). Clinical evidence of the presence of this hormone in cryptorchids, as shown by the development of the secondary sexual characteristics, has been recognized for some time. Pratt, Moore, Hinman and Meyer stated that most patients with undescended testes exhibit normal physical and mental development except for occasional psychic disturbances of the sexual power. All but 1 of the 20 adults with bilateral cryptorchidism seen at this clinic have had normal secondary sex characters. The exception had Fröhlich's syndrome.

Lipschütz stated that one sixteenth of the normal testis suffices to permit normal development of the secondary sex characters in the rabbit and the guinea pig. Judging from the small size of the gonads occasionally seen in otherwise normal cryptorchids, little testicular tissue seems to be needed to carry on this function in man.

Whether the undescended or the normal testis internally secretes more than one hormone is not definitely known, but the fact that the undescended testis has an internal secretion has been a strong argument for its conservative treatment (orchiopexy) rather than its removal (Meyer; Lotheissen).

6. *External Secretion of the Retained Testis.*—(*a*) Spermatogenesis in the undescended or incompletely descended testis. The imperfectly descended testis is often aspermatic. This is thought to be due to the influence of the higher body temperature of its abnormal surroundings on the germinal epithelium (Piana; Crew; Moore; Fukui) and also the pressure atrophy. Most experimental evidence seems to show that the undescended testis will develop normally when replaced in the scrotum. If it is too far degenerated, mature germinal epithelium will not be produced subsequent to fixation in the scrotum.

In experimental procedure a normal testis is brought up into the abdomen, allowed to degenerate, replaced in the scrotum and then seen to regenerate. It may be questioned to what extent this regeneration will occur in the naturally cryptorchid gland after orchiopexy, since the potentialities of such a gland may be entirely different from those of the normal gonad. Wangensteen has noted that restoration of the mature

germinal epithelium does not occur to the same extent after orchiopexy as after the return to the scrotum of a normal testis previously placed in the abdomen by operation.

(b) Fertility of cryptorchids. Griffiths concluded that the undescended testis is incapable of producing spermatozoa and doubted the authenticity of reports of fertility in cases in which the condition was bilateral. From a review of the literature, however, it seems clear that spermatogenesis may occur in cryptorchids. Unfortunately the details of most of the reported cases are so incomplete that one wonders whether the authors did not state impressions or prejudices as facts.

Cooper taught that patients with bilateral failure of testicular descent are like castrates. A medical student with bilateral cryptorchidism consulted him and on hearing of the probable outcome of his anomaly committed suicide. Cooper examined his testes and found spermatozoa in each. Uffreduzzi stated that 10 per cent of cryptorchids exhibit spermatozoa. Marechal found 50 cases of bilateral cryptorchidism in which examination of the testis or of the semen revealed spermatogenesis. Rawling found little if any impairment of spermatogenesis in 10 of 27 undescended testes and stated that organs situated in the inguinal, pubic and pubosacral regions exhibit spermatogenesis in from 40 to 50 per cent of persons up to 30 to 40 years. Vidal and Burghard concluded that the majority of abdominally retained testes are capable of spermatogenesis. Meyer, in a review of the literature, quoted 19 authors who stated that the cryptorchid testis is capable of producing spermatozoa and 13 who held the opposite view. In the majority of instances in which spermatozoa have been demonstrated in the undescended testis the patient has been young.

Odiorne and Simmons, Eccles, Levin and others have reported the cases of patients with bilateral abdominal cryptorchidism who apparently became fathers. Eccles stated that there are few instances of fertility in the presence of double inguinal arrest. Why abdominal retention should be more conducive to fertility is not clear.

Since Hobday stated that stud horses with abdominal testes are always sterile, the statement that abdominal retention is less inimical to spermatogenesis than is inguinal retention is probably untrue.

At the University of Minnesota Hospitals ejaculation tests have been done on 4 patients with bilateral inguinal testes and 2 with abdominal gonads. These patients have never had any treatment for their anomaly. Their ages varied from 21 to 28 years. Spermatozoa were absent from the semen of 3 with inguinal and from 1 with abdominal testes. A patient aged 24 years, with abdominally retained testes, had in the semen on one occasion only scattered sperm (1 to 3 per high power field), and these were nonmotile; he was married and

was reputed to be the father of a child. Another patient, also 24 years of age, with bilateral inguinal testes, produced motile sperm on two occasions; first there were only 4 to 5 per high power field, but at the next examination there were 1,500,000 per cubic centimeter. He was married and claimed to be the father of a child; his wife was again pregnant at the time of his last examination. Paternity tests have not been performed in either case.

Whether cryptorchids are potentially or absolutely fertile is an important question. Macomber and Saunders stated that the semen of the normal male contains between 100,000,000 and 120,000,000 actively motile spermatozoa per cubic centimeter. Rubin estimated that as many as 400,000,000 per cubic centimeter may be present. The normal count for the same person varies with illness, age, exercise, diet, mental and physical fatigue, alcoholism, endocrine imbalance and frequency of sexual intercourse. It has been estimated that normally the count does not go below 50,000,000. Twenty-five million spermatozoa per cubic centimeter have been considered but not proved to be the minimal number compatible with fertility, as approximately this number are thought to be destroyed by the vaginal secretions (Macomber and Saunders; Belding).

Macomber and Saunders reported fertility in persons with counts lower than 25,000,000. MacCollum reported his experience with 2 men each of whom had been operated on for unilateral undescended testis; the counts were 16,000,000 and 26,000,000, respectively. Both men were fathers. While repeated tests might have given counts high enough to account for the paternity, it is also possible that the figures cited as necessary for fertility are too high; certainly the number of spermatozoa is only one of the factors involved in fertilization. The nature of the associated secretions in the male and female is probably as important. I have reported an instance of paternity with a sperm count of 1,500,000, the lowest recorded in the available literature. While it is impossible actually to prove or disprove paternity, the fact that the numbers of spermatozoa supposed necessary for fertility are only estimates and the fact that only one spermatozoon is necessary for fertilization make it probable that fertility may exist in patients with sperm counts below the present accepted standards. Moreover, studies of the head, neck and tail of the sperm show that from 8 to 10 per cent may show variations in size and shape. Fertility is thought to be greatly impaired if the proportion of abnormal forms reaches 25 per cent.

To draw valid conclusions as to the fertility of bilateral cryptorchids is impossible, because too few observations have been made. However, it seems permissible to conclude that some males with bilateral cryptorchidism have not only potential fertility but also presumptive evidence

of absolute fecundity (2 of 6 of my patients). All such patients whom I have observed have been young; whether fertility exists in older patients is unknown.

7. Treatment.—(*a*) Spontaneous descent. Hofstätter stated that in 600 male newborn children 96 per cent of the testes were in the scrotum. In eight to ten days nearly all the testes were in the scrotum or slipped out of the external ring easily. If the testis fails to reach the scrotum at the end of the first year of life, it will be a rare event if it ever does so by its own initiative (Hofstätter). At the University Hospitals no spontaneous complete descent has been noted in a series of 100 imperfectly descended testes in patients aged 2 to 79 years. To be sure, there are several reports of late descent in the literature (Bühlmann; Mayor; Harris; Drake). The most interesting of these studies is that of Drake. He found that 11 of 260 boys, aged 9 to 19 years, had undescended testes (incidence, 4.2 per cent); in 4 the retained gonad was on the right side, in 6 it was on the left, and in 1 the condition was bilateral. Drake observed these boys for a period of years and found that 10 of the 12 testes descended spontaneously. If most undescended testes descend of their own accord, as Drake inferred, it is difficult to explain the incidence of 3.1 cases of ectopy per thousand men according to the draft statistics. Also, since the incidence is about twenty times the normal incidence (0.2 per cent), it is possible that the condition in a number of his cases could be classified as physiologic ectopy.

By physiologic ectopy is meant the condition in which one finds a normally descended testis with a very short or active cremasteric muscle which pulls the gonad into an inguinal or a high scrotal position. This condition, also known as ectopy en retour, has been little appreciated by most investigators. From the point of view of therapy, it is as important to differentiate it from true maldescent of the testis as it is to differentiate testicular maldescent from hernia, from benign and malignant tumors in this region or from adenitis. MacCollum noted 21 instances of physiologic ectopy in 336 cases of cryptorchidism. Of 16 patients referred to Hamilton and Hubert, only 6 were actually cryptorchids; 10 were pseudocryptorchids. Stefko in 1924 reported a high incidence (27 per cent) of inguinal testes in starving children. This he attributed to shortness of the cremaster, caused by starvation, in which an unequal growth of muscles of the abdominal wall occurs. Hofstätter described a group of 8 to 10 year old boys who could luxate their testes, pushing them into the inguinal canal and even into the abdominal cavity. On one occasion one of these boys could not replace a testicle which he had pushed above the penis, and only with difficulty could it be replaced by a physician. Bevan stated that one fourth of the

patients with retained testes referred to him do not have undescended testes, for when a finger is run down the inguinal region the testicle can be pushed into the scrotum.

To differentiate physiologic ectopy from testicular retention the following criteria may be helpful: 1. In physiologic ectopy the extremely short or active cremaster may be seen to contract. 2. The patient may state that at one time the testis was in the scrotum. 3. Physiologic ectopy is not associated with hernia as frequently as undescended testis. 4. In physiologic ectopy the testicle can be brought into the scrotum by manual traction, but when the traction is released the testicle recedes to its original position. 5. The scrotum in such cases is better developed than in cases of cryptorchidism. 6. In children with strong cremasteric reflexes the testis does not usually enter the inguinal canal but lies under cover of the loose fatty tissue which covers the front of the pubes. If the examiner palpates the region immediately below the external ring, the cord can be picked up by the fingers. When this is traced the testis will be found (Fraser). 7. If relaxation of the cremasteric and other muscles is obtained by a general method of approach and by direct application of heat to the groin, scrotum and perineum (the patient lying with his legs apart) a differentiation between pseudocryptorchidism and true cryptorchidism can be made (Hamilton and Hubert).

A sharp distinction cannot always be made between these two entities, but the history and multiple observations by different examiners will aid in the diagnosis. At the University Hospitals at least three examiners check every diagnosis of undescended testis. Physiologic ectopy may be considered to vary from true maldescent only in degree, but certainly differentiation should be made in tabulating any results of treatment.

The ultimate fate of physiologically ectopic testes has not been definitely ascertained. MacCollum gave one to understand that if such testes can be brought into the scrotum they will eventually descend of their own accord. Bevan also concluded that at puberty, when the testes enlarge, they descend into the scrotum and develop normally. Wangensteen has brought to my attention several cases which he has followed personally. Nearly all the patients had been referred for orchiopexy, but they were not operated on when the real condition was appreciated. Of 3 boys in one family, 2 had physiologically ectopic testes which descended into the scrotum at puberty and have remained there to the present time. At a recent examination the testes of both boys were normal in size, shape and position. The other boy, aged 11 years, had an inguinally retained left, testis. Another case of physiologic ectopy has been followed; when the patient was 12 years old the right testis descended into the scrotum and has remained there, but it is about half the size of its scrotal fellow.

(*b*) Surgical treatment. The surgical treatment of the undescended testis is removal, abdominal reposition or scrotal fixation (orchiopexy). Castration is justified only in certain cases of unilateral undescended testis: (1) if the patient is old and has a very atrophic testis or a large inguinal hernia, (2) if the testis is painful or (3) if the presence of a malignant tumor is suspected. Too often castration is performed because it is an easier procedure than scrotal fixation. However, it is surprising how much the cord can be lengthened by patiently separating the testis from the vaginal process, freeing the vessels and vas deferens in the retroperitoneal space even as far as the renal pedicle and separating the fascial coverings of the cord. Cutting the blood vessels of the cord to give length is to be condemned, as Mixter and MacCollum found that every patient so treated showed complete atrophy of the testes when observed from ten to twenty years later. If an inguinal testis cannot be made to reach the scrotum, abdominal reposition is preferable to castration and may be the only elective procedure for the young male with bilateral cryptorchidism.

In orchiopexy one combines the freeing of the cord with fixation of the testicle in the scrotum. Since Rosenmerkel's orchiopexy of more than one hundred years ago, numerous procedures to anchor the testis in the scrotum have been devised (see Hofstätter's outline). Over 40 operations have been described (Wolfson and Turkeltaub). The most recent ones are of the Keetley-Torek type. From many reports (Burdick and Coley; McKenna and Ewert; Ada; Gobell; Cabot and Nesbit; Tyrrell; Meyer; Eisenstaedt; Wangensteen; Newell; Wolfson and Turkeltaub and others) it is to be inferred that good anatomic results (in size, position and cosmetic effect) are obtained in most cases, even with various technics. For the past few years at the University Hospitals Wangensteen's modification of the Keetley-Torek operation has been used with uniformly good results.

In the Keetley-Torek operation the spermatic cord is freed until it is of sufficient length to allow the testicle to reach the bottom of the scrotum. The skin of the thigh is sutured to the skin of the scrotum; the testicle itself is sutured to the fascia lata of the thigh, and the wound in the scrotum is closed over the testicle. The testicle is thus kept at enough stretch so that it will remain low in the scrotum after the second stage is performed. It is important that there be no undue tension. At the second stage the scrotum is separated from the thigh and the testicle from the fascia lata, and the scrotum is closed again over the gonad. In Wangensteen's operation a cutaneous juncture between the thigh and the scrotum is made, and the testis is anchored by means of sutures which are placed in the tunica albuginea, brought down through the tunica vaginalia communis and fastened to the fascia of the thigh. The important difference in this operation is that while

fastened to the thigh the testicle is still in the scrotum. The first stage is not only more physiologic than in the original Keetley-Torek procedure but at the second stage, the scrotal-crural detachment is performed more easily and simply.

From an anatomic and from a physiologic point of view, orchiopexy is the procedure of choice in the surgical treatment of the undescended testis. It is important that the testis after orchiopexy lie free in the bottom of the scrotum and be movable. If one cannot get the testicle to the lowest portion of the scrotum, a high scrotal position is better than an inguinal one. If necessary, the testicle may be brought from its ectopic position to the scrotum in stages. Whether inguinal or abdominal reposition is the better is questionable, except that one can observe a testis better in the inguinal region. If the inguinally retained testis is painful and if conservative measures give no relief, orchidectomy may be indicated, as such a testis will probably be just as painful if placed in the abdomen. For older men, orchiopexy may be performed more for the cosmetic result than for the functional potentialities.

(*c*) Endocrine therapy—rationale. The researches of Evans, Engle, Aschheim and Zondek, Allen, Doisy and others are largely responsible for physicians' ideas regarding the hypophysial-gonadal relationship, as well as the rationale of endocrine therapy for cryptorchidism.

Allen has reviewed the effect of estrogen on the testis. While few distinctly harmful effects on the testis of the adult male follow the injection of moderate doses of estrone (theelin), degenerative changes in mature testes have been described as following the administration of large doses. In the immature male, however, it is possible to inhibit the normal growth of the spermatogenic tissue with relatively small amounts of estrogen. The testes remain infantile, sperm is not developed, and descent of the gonads into the scrotum is inhibited. The thymus gland does not undergo its usual involution. The accessory genital organs remain undeveloped. Moore concluded that these inhibitory effects may be explained by a depressing effect of the injected estrogenic substance on the anterior lobe of the pituitary gland as far as its production of a secretion essential to the normal growth and function of the testis is concerned. Burrows found that estrone tends to inhibit the descent of the testes, to prevent the testes from maturing and to induce hernia only if the testes are nearly or quite mature.

The effect of pituitary extracts on the testis is different from that of estrogen. In 1921 Engle isolated from fresh bovine anterior lobe the growth hormone of the pituitary gland. It was noted, however, that besides failure of growth, there was failure of genital development in children hypophysectomized because of a pituitary tumor and that similar retrogressive changes occurred in the genital system of adults.

The independence of the gonadotropic and growth factors of the anterior lobe of the pituitary was proved by Zondek and also by Smith, who in 1926 simultaneously detected the gonadotropic hormone of the hypophysis. They found that subcutaneous implants of anterior lobe tissue into immature rats provoked sexual maturity in these animals in from three to five days.

A more convenient source of gonadotropic substances was discovered by Aschheim and Zondek in the urine of pregnant women. It is known that estrogen is found in large amounts in the blood and urine during pregnancy and also in the placenta. It has been known for some time that the hypophysis undergoes hypertrophy during pregnancy. It was rationalized, therefore, that during gestation there would be increased secretion and elimination of the anterior pituitary gonadotropic hormone. It was subsequently found that gonadotropic substance appeared in the urine during pregnancy in large amounts and much earlier than estrogen —as early as the first three weeks of gestation, affording a diagnostic test for pregnancy (Aschheim-Zondek test).

The estrogenic substance in the urine can be separated from the gonadotropic because of the greater solubility of the former in organic solvents. Whether the gonadotropic substance in the urine is identical with the pituitary gonad-stimulating hormone has been questioned (Evans; Collip and his co-workers; Fevold and Hisaw; Zondek).

The action of the various extracts from the anterior lobe of the pituitary gland and of the urine of pregnant women has been studied in both mature and immature male animals, chiefly rats, mice and monkeys. Engle reviewed the results obtained by most of the recent workers in this field. It was noted that while injections of whole urine of pregnant women caused hypertrophy of the accessory sex apparatus, no constant change in the size of the testis occurred, and while the interstitial mass was increased, there was no acceleration of spermatogenesis. The only uniformity of agreement among investigators on the response to extracts of the anterior lobe or to the gonadotropic substance from the urine of pregnant women is that premature development of spermatozoa has not been demonstrated and that animals which have been treated do not mate. Thus the acceleration of development and even maturation of the genital system should not be considered synonymous with sexual maturity (Moore). Engle summarized the data acquired through the study of a series of animals, both rats and monkeys, as follows: 1. The testicular weight of animals treated with either concentrated urine of pregnant women or with pyridine extracts of sheep glands is considerably increased. 2. The increase in the interstitial mass after the use of anterior pituitary extract is slightly greater than in the untreated control, but after the use of concentrated urine

of pregnant women it is greatly increased. 3. Neither of these degrees of change has been noted to follow fresh implants. 4. The failure to induce acceleration in spermatogenesis is uniform with the findings after implantation, although the size of the tubules is greater than in the controls or the rats receiving implants.

Engle also found that injections of extracts of urine from pregnant women and water-soluble extracts of the anterior lobe of the pituitary gland produced descent of the testes in 10 immature macaques. Normally the male macaque exhibits at birth turgescence of the scrotum and descended testes. Shortly after birth the testes ascend into the inguinal ring, while the scrotum regresses until it becomes a flattened fold of skin between the thighs. Not until the third to the fifth years do the testes descend again permanently, at which time the scrotum becomes fully formed (Wislocki). In the monkeys treated by Engle the testes grew, and during the course of treatment the scrotum increased in size even before the testes had descended into it. The same author noted the similarity between the scrotal response in monkeys and that in newborn human children. Since in the human male the testes are descended at birth and in the human female the gonadotropic principle is in the circulation throughout the period of gestation, Engle postulated that the hormone is involved in the descent of the testes in the human male.

Aberle and Jenkins injected about 2,575 rat units of the gonadotropic principle from the urine of pregnant women into each of 6 monkeys. The testes enlarged, but only a single testis descended to the lower part of the scrotum. Biopsy of the testes showed tubular enlargement and increase in interstitial tissue but no mature spermatozoa. Grossly, there was shortness of the fascia surrounding the vas deferens and spermatic vessels, which was believed to be responsible for lack of complete descent. They stated that Engle used monkeys that were heavier and therefore probably older and more mature. Unfortunately, the amount of gonadotropic substance given by Engle was not stated. According to Aberle and Jenkins, identical amounts of the gonadotropic substance from the urine caused various degrees of hypertrophy in the prostate, seminal vesicle and testes of immature monkeys.

Smith and Leonard, who used gonadotropic substance from the urine of pregnant women (antuitrin-S) in hypophysectomized rats, stated that spermatids and even sperm may be found, though none was present at the beginning of treatment. When injections were begun at the time of hypophysectomy the regression in the weight of the testes was slowed, and enlargement sometimes was found. Atrophy of the tubules was retarded, and mature spermatozoa continued to be present longer than in the hypophysectomized litter mates. Smith and Leonard concluded that in pituitary insufficiency injections of urine from pregnant women might have a beneficial effect on spermatogenesis.

That the testes influence the activity of the pituitary gland has been shown by many investigators. Severinghaus, Engle and Smith, in their review of the literature, related the histologic changes in the anterior lobe of the hypophysis following castration in the male or female. One is impressed, however, with the fact that the changes are not identical in all species. The hypophysis of the castrated rat shows a marked increase in basophils, while the same organ in the castrated man, horse, ox, pig, cat, dog, guinea pig, rabbit or domestic fowl is said to show an increase in eosinophils. Nelson found that as the testes of the experimentally cryptorchid rat underwent degenerative changes the hypophysis also exhibited changes which were similar to those found after castration. The injection of gonadotropic substance from the urine of pregnant women (antuitrin-S) into these animals resulted in stimulation and restoration of the seminal vesicles and of the prostate, while the hypophysis showed a disappearance of castration cells. There was no change in the epithelium of the seminiferous tubules, but the interstitial tissue of the testis showed marked stimulation. The treatment of a series of castrated rats with gonadotropic factor extracted from the urine of pregnant women resulted in no change in the hypophysis or in the accessory sex glands. Nelson concluded that the testis plays an intermediary role in the influence exerted on the pituitary and accessory sex glands.

Evans and Simpson, and Collip, Selye, Anderson and Thomson, working with laboratory animals, have shown that the combined use of an alkaline extract of the anterior lobe of the pituitary gland and gonadotropic substance from the urine is more effective than the use of either alone, the former activating or enhancing the gonadotropic principle by its synergistic action. Smith and Leonard, Evans, Pencharz and Simpson have shown that a pituitary extract from the urine of pregnant women may produce stimulation of the germinal epithelium of the testes, but maximal or complete results were obtained in their work by a combination of the pituitary extract and gonadotropic substance from the urine of pregnant women. The anterior pituitary substance does not seem to bring about complete spermatogenic maturation of the testis, as the work of Engle, Rubinstein, Aberle and Jenkins has shown. The studies of Schockaert, Brosius and Schaefer, and Kraus seemed to suggest this possibility, but it was not conclusively proved that their experimental subjects did not display this function before treatment.

There are several series of human undescended testes which have been treated with the gonadotropic substance from the urine of pregnant women. A report of these cases and the results of treatment in similar cases at the University Hospitals will be discussed later.

8. *Results of Treatment.*—(*a*) Function after glandular therapy. There are no controlled reports in the literature in which an aspermatic undescended testis is said to have shown active spermatozoa after treatment with the gonadotropic substances from the urine of pregnant women. The results following the injection of serum from pregnant mares will be discussed later. If there is a potentially active germinal epithelium in the undescended testis, it is theoretically possible that descent induced by the gonadotropic substances mentioned might result indirectly in spermatogenesis as a result of better (scrotal) position.

(*b*) Function after surgical treatment. In the available literature there are only 2 series of cases in which the functional results following orchiopexy have been recorded. In 1935 Wangensteen reported that, of 6 patients with bilateral failure of descent, spermatozoa were found in the semen of 4 after orchiopexy. In no case was the number of spermatozoa per cubic centimeter as high as in the normal person. MacCollum found that 82 per cent of 22 patients with bilateral undescended testis operated on at the Children's Hospital, Boston, were fertile after operation. When one considers that only about 10 per cent of untreated cryptorchids show spermatogenesis (Uffreduzzi), the value of operative treatment is apparent. It would be more real, however, if one knew (1) how long an untreated cryptorchid may remain fertile, (2) the sperm count before and after orchiopexy and (3) the histologic appearance of the testis before and many months after scrotal anchorage (see Wangensteen's case).

II. SCOPE OF THIS STUDY

The purpose of this study is to determine how closely the functions of the undescended testis approach those of the normally descended gland, both before and after fixation in the scrotum.

Although orchiopexy has been performed for more than a century, few investigators have inquired whether the undescended testis has any function, or, if function exists, whether it can be maintained or improved by scrotal fixation. From the evidence in the literature it seems established that undescended testes have an internal secretion and occasionally possess an external secretion sufficient for potential, if not absolute, fertility.

Knowledge of the functional capacity of the undescended testis is important as a basis for rational treatment. It is generally agreed that in most mammals maldescent of the testis, whether congenital or experimental, progresses to atrophy after puberty. Conclusions concerning the results of treatment have been based on both clinical and experimental cryptorchidism. However, there are limitations to the clinical investigation of a problem of this type. Also, it may be questioned to what extent one is justified in drawing conclusions from researches based on

experimentally cryptorchid subjects in which the potentialities of the normal gland were originally present. As has been mentioned, the potentialities of the congenitally undescended gland may be entirely different.

III. TESTICULAR MATERIAL INVESTIGATED

In the experimental study of this problem only naturally cryptorchid animals, chiefly the dog and the pig, were used, unless otherwise specified. In these animals cryptorchidism is not infrequent. While working in the experimental laboratory of the department of physiology of the University of Illinois Medical School, I noted 7 instances of undescended testis (in 2, bilateral) in 200 dogs. At the stockyards of Armour and Company, South St. Paul, Minn., during one of the morning "kills," 4 instances of retained testes were noted in approximately 2,000 pigs. In this investigation the naturally occurring cryptorchid testes of 26 pigs and 15 dogs were studied. In the operative procedures, pentobarbital sodium (35 mg. per kilogram of body weight), injected intraperitoneally, and drop ether were used as the anesthetics. Sterile precautions were used in the surgical operations.

IV. OBSERVATIONS IN ANIMALS AND MAN, WITH PERTINENT CITATIONS FROM THE LITERATURE

1. *Histologic Appearance of the Undescended Testis.*—In this laboratory congenitally undescended testes have been studied histologically in the pig, dog, horse and bull. The microscopic appearance of the retained testis in each of these animals is similar to that in man and is comparable to that in cases of experimental cryptorchidism (table 1 and figs 1 and 2). The testes are ordinarily smaller than normal, their tunics are usually thicker, and the cut sections are darker and more fibrous. They contain seminiferous tubules in which only Sertoli cells may be visible. Some cells of the germinal line are found, but there is never a complete germinal epithelium if the testes have been entirely confined to the abdomen. Testes located in the inguinal region or the upper part of the scrotum may occasionally contain spermatozoa, but this is rare in the adult animal, according to Moore.

In this study the microscopic sections never showed spermatozoa in the lumens of the seminiferous tubules of congenitally abdominal or inguinal testes whether these were from adult man, pig or dog. Botschi described the appearance of congenital undescended testes in the pig, horse, dog and cat. He found that in these animals the greater number of retained testes are aspermatic and that even spermatocytes are seldom found. Wangensteen concluded that the germinal epithelium is better maintained in the undescended gonad of the horse than in that of man, pig, dog or bull.

In most animals the empty tubules are more widely separated in the undescended than in the scrotal testis. The amount of interstitial tissue varies in different animals. The interstitial mass of the cryptorchid

boar is so prominent that Bouin and Ancel designated such tissue the "interstitial gland." The interstitial cells are less evident in the ram (Moore).

2. *Spermatozoa in Smears and Sections of Descended and Undescended Testes.*—(*a*) Pigs. The following study concerns abdominal

Fig. 1.—Section of a congenitally undescended canine testis (× 700). Note the tubular degeneration, the increase in interstitial tissue and the lack of spermatozoa in the lumens of the tubules.

testes in 11 full grown pigs, obtained through the courtesy of Armour and Company, South St. Paul, Minn. Smears were made from cut sections of the testis, epididymis, vas deferens and seminal vesicles and were stained with iron hematoxylin and methylene blue. Microscopic

sections were then made from each of these organs and from the prostate and were stained with hematoxylin and eosin. Both smears and sections were searched for spermatozoa, and the germinal epithelium was scrutinized.

Fig. 2.—Section of the inguinally retained left testis (× 700) of an adult dog (dog 1, table 1) after scrotal fixation for three months. Degeneration and atrophy are still apparent; there is no evidence of germinal maturation. There is little difference between this treated testis and that shown in figure 1.

The gonads in every case revealed the usual degenerative changes. In none was there a mature germinal epithelium. There was marked increase in the interstitial tissue. However, smears made from cut sections of the testes revealed spermatozoa in 6.

Although the smears of the epididymis and seminal vesicles in 2 instances showed spermatozoa while the microscopic sections did not, this was probably due to the manner of preparing the slides. As controls, sections and smears were made of the testis, epididymis, vas deferens and seminal vesicles of 3 adult boars. In all instances spermatozoa were seen in sections of the testis and epididymis and in smears of the testis, epididymis, vas deferens and seminal vesicles.

The finding of spermatozoa in abdominal testes of pigs raises the question of fertility. Hobday represented most veterinarians as considering animals with abdominally retained testes sterile but reported finding spermatozoa in 2 of 14 abdominal testes and in 5 of 11 inguinal gonads from horses. In the present study smears of the cut surfaces of testes from 11 cryptorchid pigs yielded spermatozoa in 6.

From the foregoing data it would seem that in some of the lower animals potential fertility may exist for a longer period than is generally believed.

(*b*) Man. A similar study was carried out with the normally descended human testis. At postmortem examination, smears and sections were made from the cut surface of the testis and occasionally from the epididymis, vas deferens and seminal vesicle. The former were stained with methylene blue and the latter with hematoxylin and eosin. In 18 consecutive autopsies on male patients smears and sections were made of 32 adult descended testes; the smears of 6 of these testes contained spermatozoa, but the sections did not. Histologically the testes often appeared disorganized, probably because of the infection from which many of the patients died. That illness may have an unfavorable result on spermatogenesis has been stressed by Wangensteen.

This and the studies on the pig indicate that smears from cut surfaces of the testis or seminal vesicle are a far more reliable index of the presence or absence of spermatozoa than are histologic sections of the testis. It is interesting that such poor-appearing germinal epithelium may elaborate spermatozoa. While some areas of the gonad may appear more nearly normal than others, my studies of cryptorchid pigs show that the germinal epithelium is never as mature as that in the normal gland.

3. *Hypophysis of the Naturally Cryptorchid Pig.*—It has been previously mentioned that in experimental cryptorchidism the hypophysis undergoes changes similar to those seen after castration. Fortunately, hypophyses were obtained in 5 cases of undescended testes of adult pigs. In 2 cases the maldescent was bilateral. The sections were fixed in Zenker's solution and were stained by Mallory's modification of the azocarmine stain. Dr. A. T. Rasmussen of the department of neurology of the University of Minnesota School of Medicine reviewed the slides

and agreed with me that there is no evidence of castration cells (vacuolated basophils) in the pituitary gland of any of these 5 animals. The histologic character of these glands as to type and number of cells was by him considered normal. In each of the 3 cases of unilaterally retained testes the other testis had been previously removed, presumably by castration. Sections of these 7 undescended testes (2 bilateral, 3 unilateral) revealed no mature germinal epithelium. Smears of the testes in the two cases of bilateral maldescent failed to show spermatozoa. It seems logical to conclude that either (1) there was some other endocrine balance which kept the hypophysis morphologically normal or (2) the changes seen in the hypophysis in experimental cryptorchids are not the same as those seen in cases of naturally occurring undescended testes. In this connection Dr. Rasmussen has called my attention to a recent autopsy performed at Ancker Hospital, St. Paul, Minn. The patient was a man 34 years of age, who had died of pulmonary tuberculosis. The testes were scrotal but underdeveloped and hypoplastic, measuring about 1 cm. in diameter. Microscopic examination revealed an atrophic germinal epithelium, yet the hypophysis in this case was normal histologically. The prostate was also of normal size.

From the foregoing data one begins to wonder how necessary and direct the hypophysial-gonadal relation always is. Also it may be questioned what benefit would be derived in such a case from the use of the gonadotropic substance from the urine of pregnant women in the treatment of undescended testes.

4. *Tissue Culture of Undescended and Descended Testes of Man and Dog.*—Theoretically, the best way to study the histologic potentialities of any organ is by tissue culture. In the available literature there is no report of tissue culture of the naturally undescended testis. Goldschmidt, Fischer, Champy and Esaki have reported the results of culture of testicular tissue of various species. Esaki studied cultures of testicular tissues from normal guinea pigs and rabbits and from animals in which cryptorchidism had been produced experimentally. Levi in 1934 gave the most complete review of the subject to date.

The various studies seem to indicate that the epithelial nature of testicular cells is less definite in tissue culture than that of the germinal cells of the ovary. In cultures of the testes of the rabbit, the Sertoli cells change into large round cells which will phagocytose carmine and the germinal elements. Esaki found that the Sertoli cells in cultures of testes from rabbits with experimentally produced cryptorchidism became fibroblastic. In fact, dedifferentiation to fibroblastic tissue took place readily. The interstitial cells are not phagocytic and must be sharply differentiated from the histiocytes. They are transformation products of undifferentiated mesenchyme and under favorable conditions can change into fibroblasts. The difficulties and limitations of working with

a greatly differentiated tissue like that of the testis are apparent to any one who has made tissue cultures. However, it was thought that a comparison of the line of development in cultures of descended and of naturally ectopic testes might be helpful in elucidating the potentialities of these two types of organ.

Through the cooperation of Dr. Joseph King of the department of physiology at the University of Minnesota School of Medicine, cultures were made of tissues from 3 undescended human testes, 4 decended human testes, 1 naturally undescended canine testis, 2 descended canine testes and 3 normal, descended testes of rabbits. These tissues had been removed under sterile precautions. In each of 2 of the cases of undescended human testes a small slice of gonad was removed for tissue culture at orchiopexy. In the third case an orchidectomy was performed because of the small size of the testes and the large associated inguinal hernia.

The slide technic was used, with heparinized rabbit plasma and embryonic tissue extract (chick) as mediums. One of the cultures of the descended canine testes had to be discarded because of contamination. The series were comprised of single and multiple plants of fragments varying widely in size. The growths were carried for periods of five to sixteen days, being fed every third day with the tissue extract and plasma mentioned. There was no lysis of the clot. The cultures were all sterile at the end of the experiments. Sections and whole plants were fixed at various intervals and stained with Heidenhain blue.

The results are given in table 2. In general, in both the human and canine series fibroblasts were seen early (within forty-eight hours). The cultures were on the whole predominantly fibroblastic, even though the amount of tissue extract was varied in some cultures. The rate of growth was slow, as would be expected in adult tissue. In many of the cultures round clear cells appeared at the periphery, which have not been definitely identified. No studies on the phagocytosis of dye were made. In some of the sections there were many polyblastic cells. The epithelial nature of the tissue was not apparent in any of the growths. In neither the descended nor the undescended testes series did characteristic or specific germinal cells develop (fig. 3).

In the explant of the rabbit testis great masses of cells were seen pushing their way out from the edge. In general, these masses were darkly granular at the center and were covered at the outer surface with from one to three layers of clear, round cells, varying between 18 and 28 microns in diameter. They were regularly arranged and suggested a vertical section through an epithelial membrane. In these cultures there were also free cells, some of which were ameboid, which were probably related to the clear, round cells mentioned.

It should be pointed out that there is an unusual tendency for normal testis, especially rabbit testis, to coagulate when fragmented. This may be overcome by extensive and rapid serial dilution.

In comparing the cultures of the descended and undescended testes of man and of the dog, there was no absolute sign of differentiation in

TABLE 2.—*Results of Tissue Culture of Testes*

Source	Patient	Age	History	Treatment	Histology	Duration of Culture	Results
1. Human undescended testis	1 (E. R.)	26 years	Left indirect inguinal hernia and inguinal retained testis	Orchiopexy plus biopsy plus culture; hernioplasty	Atrophic testis	19 days	Active fibroblastic growth; no specific cells; many free cells along edges—"amebocytes"
2. Human undescended testis	2 (L. M.)	34 years	Right indirect inguinal hernia plus undescended testis at extreme right	Orchidectomy plus culture; hernioplasty	Atrophic	15 days	Active fibroblastic growth; no specific cells; "amebocytes"
3. Human undescended testis	3 (M. L.)	6 years	Left inguinal retained testis plus inguinal hernia	Orchiopexy plus biopsy plus culture	Prepubertal	1 day	Good fibroblastic growth and some round, clear cells; "amebocytes," no differentiation
4. Human descended testis	4.	21 years	Hydrocele, right	Orchidectomy	.....	6 days	Cultures showed fibroblasts and a few "amebocytes"; a few rather irregular cells with 1 or 2 processes (fibroblasts in mitosis)
5. Human descended testis	.....	.....	Hydrocele	Orchidectomy	.....	13 days	Fibroblastic cellular periphery; "amebocytes"; proliferating polyblasts
6. Human descended testis	.....	.....	.....	.....	.....	7 days	Fibroblastic
7. Human descended testis	.....	.....	.....	Orchidectomy	.....	8 days	Fibroblastic, branched forms
8. Canine descended testis	.....	Adult	.....	.....	Normal	6 days	Slow growing fibroblasts
9. Canine descended testis	.....	Adult	.....	.....	Normal	2 days	Contaminated
10. Canine undescended testis	.....	Adult	Abdominal retained right testis 2 by 1.5 by 1.5 cm.	Orchidectomy	.....	5 days	Fibroblasts; peculiar stellate cells; polyblasts
11. Rabbit descended testis	.....	Adult	.....	.....	.....	6 days	Fibroblasts, "amebocytes"; stellate cells; epithelial strands
12. Rabbit descended testis	.....	Adult	.....	.....	.....		
13. Rabbit descended testis	.....	Adult	.....	.....	.....		

either series. It should be stated that 2 of the human retained gonads had an atrophic appearance histologically, while the other had the microscopic characteristics of a prepubertal gland. The growths for the most part were fibroblastic and nonspecific. Only in the rabbit series was the epithelial nature of the culture apparent. There was no marked

Fig. 3.—Tissue culture of an undescended human testis (case 1, table 2). Note the fibroblasts; at the periphery of the growth are darker round cells, one of which is in mitosis. No specific cell types are seen.

difference between cultures representing descended and undescended gonads. This may mean that undescended and descended testes have the same fundamental potentialities, but in view of the lack of positive differentiation one should not rationalize too far. All that can be said

at present is that there does not seem to be any difference in the line of development in tissue cultures representing descended and naturally cryptorchid testes.

5. *Effect of Ligating Between the Testes and the Epididymis of the Dog.*—In this clinic studies have been made of the undescended testis to note any abnormality in the pathways for seminal transmission. If such a defect exists, its relation to the degenerative changes in the ectopic testis is of speculative interest. While it is established that the imperfection of the cryptorchid testis is due partly at least to the thermal and pressure effects resulting from its abnormal position, it has never been denied that some undescended testes are anatomically malformed ab initio (Wangensteen). A common finding in the undescended testis is the separation of the epididymis from the testis. How often this occurs normally is unknown. As mentioned before, the undescended testis is often smaller than its scrotal fellow.

My interest in this subject was increased by the inability on 6 occasions to find a supposedly retained testis at operation.

Case 1.—L. H., a boy aged 8 years, was admitted to the University Hospitals on June 4, 1930 and discharged June 17.

On admission the diagnosis was bilateral undescended testis, present since birth.

On physical examination the left testicle could not be palpated, but the right testicle could be felt in the inguinal canal. It was freely movable but could not be brought into the scrotum.

When the patient was operated on, the gubernaculum was seen to come down posterior to the parietal peritoneum and to embed itself deep to the Poupart ligament. There was no definite evidence of testis. Exploration of the retroperitoneal space and peritoneal cavity with the finger revealed no testis. A small hernial sac was felt.

Microscopic sections of the tissues removed showed several lymph nodes, gubernaculum and vas deferens. A hernioplasty was performed on both sides and an orchiopexy on the right.

Case 2.—W. O., aged 16 years, was admitted to the University Hospitals Oct. 15, 1935, and was discharged November 11. Since birth he had had undescended testes. He had never noticed the testes in the scrotum or felt them in the canals. The family physician had made an injection into the left inguinal canal for hernia.

Physical examination revealed the penis and scrotum to be somewhat underdeveloped. The testicles were not felt in the scrotum or in the inguinal region. The patient had a congenital cardiac lesion, probably on the basis of pulmonary stenosis. His general appearance was that of a cretin.

A prostatic smear produced no spermatoza. The basal metabolic rate was + 6 per cent.

On October 18, exploration was done through a right oblique inguinal incision. No testis was found. Dissection was made into the retroperitoneal region as far as the bifurcation of the aorta. The peritoneal cavity was opened also, but no trace of testis, vas deferens or gubernaculum was found. A hernioplasty was performed, and the wound was closed. On November 11 an orchiopexy was performed on the left side.

CASE 3.—A. B., aged 24 years, was admitted to the hospital June 13, 1935, and discharged June 25. The patient said that the left testicle had never been felt. The right testicle had always been normal in size and position. No hernia could be demonstrated on physical examination, nor could the left testicle be palpated.

On June 14, through a left inguinal incision, the region was explored. There was a spermatic cord, in which the vas deferens and vessels were found. No testis was found. The retroperitoneal space was explored. No testicular tissue being found, the vas deferens was amputated near the bladder and the spermatic cord cut high in the retroperitoneal region. A small hernial sac was found, which was ligated. A Bassini hernioplasty was done in the usual fashion.

CASE 4.—R. U., aged 11 years, was admitted to the hospital July 24, 1935, and discharged August 7. The patient had a right inguinal hernia and bilateral undescended testis. One year previously a herniorraphy had been performed on the right side in another hospital, at which time no right testis was found.

On July 25 the patient was operated on, and a recurrent right inguinal hernia was repaired. A normal spermatic cord was found, but no definite testis was isolated. In the retroperitoneal space there was a small piece of tissue that was thought to be testis, as there was a small vascular pedicle running from it toward the renal region. This tissue and the spermatic cord in the inguinal region were removed for histologic study. A hernioplasty was performed according to Andrews' technic.

Microscopic sections of the removed tissue showed fibrous tissue, blood vessels and a small lymph node.

CASE 5.—W. R., aged 20, was admitted to the hospital March 16, 1938, and was discharged March 28.

The patient had had undescended testes since birth. A year previously the family physician had tried gonadotropic substance (antuitrin-S), with no results.

The right testis could be felt overlying the external oblique aponeurosis, having migrated out to the external abdominal ring. There was an indirect inguinal hernia. A testis could not be felt, nor was there a hernia on the left side.

A right orchiopexy and hernioplasty had been performed on Dec. 3, 1937.

The patient returned March 16, 1938, at which time the scrotal-crural anastomosis on the right was undone and exploration was carried out through a left oblique inguinal incision. The conjoined tendon was intimately attached to the external oblique aponeurosis at Poupart's ligament. There apparently was no vas deferens. A tiny remnant of a structure deriving from the bladder on the outside of the peritoneum may have represented the vas deferens. The gubernaculum extended into the scrotum. No testis or spermatic vessels could be found.

A hernioplasty was performed.

Microscopic sections of the tissues removed revealed probable vas deferens, fibrous tissue and blood vessels; there was no testis.

CASE 6.—G. S., aged 8 years, was admitted to the hospital Aug. 12, 1930, and discharged August 23. For two years prior to his admission it had been noted that the left testis of the patient was not in the scrotum. At no time had the condition caused him any discomfort.

Physical examination gave essentially negative results except that no left testicle could be felt. The right testis was normal in size, shape and position. The external genitalia were normal.

On August 13 an operation was performed. When the external oblique aponeurosis was divided the terminal end of the spermatic cord was seen to insert

into the outer leaf of the external oblique aponeurosis. It did not extend into the scrotum. With the slightest traction it was detached. When this was followed medially the vas and spermatic vessels were seen, both of which were extremely small. What seemed to be testis and epididymis were mere nubbins of tissue, about one-fifth or one-sixth the size of the other testis. This tissue was removed, but on cut section it proved to be scar tissue. No testis was found. An indirect inguinal hernia was repaired.

Microscopic study of the removed tissue showed no evidence of testicular tissue. Epididymis, spermatic cord, spermatic blood vessels, muscle and fibrous connective tissue (gubernaculum?) were present.

These 6 cases are examples of probable monorchism, and the incidence of 6 in a series of 143 cases of cryptorchidism seen at this clinic to date is of questionable significance. Theoretically, if one considers the undescended testis to be congenitally imperfect, one would expect to find a gradation from anorchism to almost perfection. However, most of my cases would belong to the group showing the upper stages of development. Moreover, up to puberty it is impossible to differentiate grossly or microscopically between the descended and the retained testis. Knowing the effects of an extrascrotal environment on the testis, it seems safe to say that the retained testis is not necessarily congenitally imperfect, but that it may become degenerate as a result of its abnormal position.

The possibility that the degenerative changes in the ectopic testis may be due to some defect in the pathway of seminal transmission has been suggested. In the available literature, however, there is no report of any obstruction or lack of continuity in cases in which the testis, epididymis and the cord have been present. In this laboratory, attempts to force mercury and colloidal dyes through the duct system of the epididymis from the vas deferens have been unsuccessful in both normal and undescended testes. This is probably due to the secretion in the lumens, the size of the ducts and the winding arrangement of the tubules.

The work of Moore and other investigators seems to prove that occlusion of the ductus deferens leads neither to testicular degeneration nor to interstitial hypertrophy. Van Wagenen, Oslund, Cunningham and Knaus concluded that closure of the ducts issuing from the testis (vasa efferentia) leads to destruction of the germinal epithelium. Moore, however, questioned this, since testicular grafts recovered six months after transplantation of immature testes show spermatozoa. He believed that he had conclusive evidence against this view, since he had examined a guinea pig with congenital absence of the wolffian duct. The testes of this animal were normal in size and appearance and occupied a scrotal position. One testis lacked vasa efferentia, the epididymis and a portion of the vas deferens, which did not reach the urethra. No seminal vesicles were present. The testis which had never had vasa efferentia or the epididymis showed approximately 50 per cent of the

seminiferous tubules in a normal state, with quantities of spermatozoa. Moore stated that since production of germ cells continues even in the absence of vasa efferentia, occlusion of these ducts cannot be held responsible for testicular degeneration. Moore's work has been criticized, however, in that the evidence which he presents is inferential and not direct.

Most of the aforementioned experiments were performed on rats, cats, mice, rabbits and guinea pigs. The following experiments were performed to study the effect of ligating between the epididymis and the testis of the dog.

Twenty-one animals were studied. Healthy adult dogs, weighing from 11 to 25 Kg., were anesthetized with pentobarbital sodium. In 12 cases, the testis on one side was exposed, and under aseptic precautions a silk ligature was placed where the epididymis and the testis joined. In the other 9 cases this juncture was cut across between silk ties. The opposite testis was also exposed and manipulated at the same time, as a control. After material for biopsies had been taken, the testes were placed in the scrotum. At periods of from two days to eleven months the testes were removed and studied. It should be stated that attempts were made not to compromise the blood supply of either the testis or the epididymis, but some vessels unavoidably were included in the ligatures. After the ligation the testes in every instance were firm, tense and congested in color. Fifteen of the organs were removed after periods of from seven to eleven months. The testis on which operation had been done in these 15 cases was always smaller and more atrophic than that on the control side, and its capsule was much thicker. However, on microscopic examination, except for fibrosis and tubular atrophy near the periphery of the testis, which was probably an effect of pressure, there was no noticeable tubular degeneration or increase in interstitial tissue as compared with the control testis and other normal testes. No relative or absolute histologic differences could be ascertained between the two series except that in the cases in which operation was done the cells lining the tubules were larger and darker-staining than those of the control testis. There were numbers of spermatozoa in the lumens of some of the tubules of the testes with obstruction (table 3).

These experiments would tend to confirm Moore's statement that occlusion of the efferent ducts of the testis does not result in testicular degeneration. Evidently spermatogenesis can exist even with no efferent pathways of the testis. The significance of this finding in attempts to explain the degenerative changes in the ectopic testis as a result of some defect in the pathway of seminal transmission, even if present, is at once apparent.

6. *Quantitative Study of the Interstitial Cells of the Undescended Testis.*—In the literature it is said that a compensating hypertrophy of the interstitial tissue occurs in the cryptorchid testis (Bouin and Ancel), but whether this increase is relative or absolute has never been accurately determined. Bascom in a critical review gave a method for determining the relative amounts of interstitial and tubular tissue in

TABLE 3.—*Effect of Tying Between Epididymis and Testis in Dog*

Dog No.	Weight, Kg.	Side on Which Operation Was Done	Duration of Ligation	Results—Treated Testis		Results—Control Testis	
				Gross	Microscopic	Gross	Microscopic
1	21.0	Left (ligation)	2 days (dog died)	.....	Some disorganization and giant cells in tubules; tubules not as cellular	.....	Fairly normal
2	13.7	Left (ligation)	1/8/35 3/14/35	⅔ size of right testis; tunica adherent; skin and subcutaneous tissue ¾ inch (2 cm.) thick	Tubules full; dark-staining round cells; tubules smaller; some tubules normal; sperm present	Capsule slightly thickened	Some disorganization in tubules
3	14.0	Left (ligation)	1/9/35 10/5/35	Testicle embedded in scar tissue; blood supply normal	Atrophy toward periphery; centrally normal	....	Normal
4	12.3	Left (ligation)	1/9/35 12/4/35	Very atrophic	2 mo. later biopsy showed atrophy and separation tubules; at 11 mo., still some atrophy but picture improved	.....	At 2 mo., atrophy and disorganization; at 11 mo., practically normal
5	22.0	Right (ligation)	1/11/35 3/12/35	Skin, subcutaneous tissue and tunica 0.75 cm. thick; testis atrophic and fibrotic	Marked atrophy	.....	Normal; approximately same as biopsy at operation
6	25.0	Left (ligation)	1/11/35 11/6/35	Slightly smaller than right	2 mo., slightly disorganized but fairly normal; 10 mo., normal	.....	2 mo., gland disorganized, but fairly normal; 10 mo., normal
7	12.0	Left (ligation)	1/21/35 11/13/35	.....	2 mo., slightly disorganized and atrophied; 10 mo., fairly normal	.....	10 mo., normal
8	11.0	Right (ligation)	1/26/35 12/5/35	.....	Atrophy at periphery; normal in center	.....	.....
9	12.0	Left (ligation)	1/29/35 2/1/35	Dog died of peritonitis; cholecystectomy	Disorganized	.....	Disorganized
10	25.0	Left (ligation)	2/8/35 11/7/35	Epididymis was separated from testis at operation	Atrophic at periphery; centrally normal	.....	Normal
11	18.0	Left (ligation)	2/12/35 2 14/35 (distemper)	.....	Disorganization	.....	.....
12	15.0	Left (ligation)	2 2)/35 11/7/35	.....	Fairly normal	.....	Normal
13	12.5	Left (division)	3/13/35 11/13/35	.....	Tubules have larger and darker staining cells; atrophy toward periphery; otherwise fairly normal	. .....	Atrophy toward periphery, normal centrally
14	16.4	Left (division)	3/26/35 10/5/35	.....	Normal; numerous spermatozoa	. .....	Normal
15	....	Left (division)	3/26/35 10/30/35	.....	Normal; deeper stained	.....	Normal
16	....	Left (division)	3/26/35 12/5/35	.....	Normal cells in lumens of tubules larger and darker stained	.....	Normal
17	....	Left (division)	3/26/35 10/30/35	.....	Normal	.....	Normal
18	....	Left (division middle)	4/2/35 11/12/35	.....	Normal	.....	Normal
19	15.0	Left (division middle)	4/2/35 11/12/35	.....	Normal	....	Normal
20	12.3	Left (division)	.....	.....	Normal	....	Normal
21	11.0	Left (division lower ¾)	4/2/35 1/2/36	.....	Normal	....	Normal

the testes and denied that a compensatory hypertrophy of the interstitium occurs in the testis of the naturally cryptorchid pig. He based his conclusions on studies of unilaterally cryptorchid animals in which the other testis was absent, presumably as a result of castration. For this reason his work was not adequately controlled.

In this study, full grown dogs (except dog 5, which was young) were rendered cryptorchid, and the amounts of interstitial and tubular tissue were determined to see if there was a relative or an absolute change in the amount of interstitial tissue. With the animal under pentobarbital sodium anesthesia, the right testis was exposed, and after material for biopsy had been taken the gonad was placed in the inguinal region or in the abdomen. After three months, both the right testis and the left (control) testis were removed. Histologic sections were made and stained with hematoxylin and eosin. A drawing of a representative field from a section of each testis was made with a projection apparatus. Tracings of these sketches were cut out with scissors, and the tubular and interstitial areas were weighed separately. From these weights the relative percentages of the two tissues were estimated. The weight of the testis being known, the weights of the interstitial tissues and the tubules could be calculated. The results of the calculations are given in table 4.

Of 11 dogs in which cryptorchidism was experimentally produced 7 showed an increased percentage of interstitial tissues in the "undescended testis" after three months of abdominal or inguinal retention as compared with the control gonad, 3 exhibited a decrease, and 1 (dog 11) showed practically no change. In all cryptorchids except dog 3 there was a decrease in the actual weight of the interstitial tissue of the abdominal or inguinal testis. This would tend to show that in experimentally produced cryptorchidism the increase in interstitial tissue is relative and not absolute, the relative increase being due to the tubular degeneration and the absolute decrease being due to the generally smaller size and weight of the gonad. Whether these deductions hold true for the testis of the naturally cryptorchid dog is unknown. Bascom and Moore pointed out that there are variations in the amount of interstitial tissue in different species. Also, Moore called attention to the danger of speculating as to the degree of function from the amount of interstitial tissue.

7. Effect of Serum from Pregnant Mares on the Testis of the Cryptorchid Dog.—Wells reported the effect of serum from pregnant mares on the reproductive organs of a hermaphrodite ground squirrel. Subcutaneous injection of the serum in a dose of 25 rat units twice daily for eighteen days caused precocious production of spermatozoa in the right ovotestis, which descended to the scrotum, and also induced the formation of graafian follicles and corpora lutea in both ovotestes. All the male accessory reproductive organs of the hermaphrodite showed great stimulation, probably owing to the stimulation (by gonadotropic substance) of the animal's own ovotestes to release male hormone. In

TABLE 4.—*Relative Amounts of Tubular and Interstitial Tissue in Undescended Canine Testis*

		Right Testis						Left Testis						
				Tubular Tissue		Interstitial Tissue				Tubular Tissue		Interstitial Tissue		
Dog	Weight, Kg.	Weight, Gm.	Size of Testis, Cm.	%	Gm.	%	Gm.	Weight, Gm.	Size of Testis, Cm.	%	Gm.	%	Gm.	Position of Right Testis
1	16.8	12.55	4×2.5×2	77.0	9.66	23.0	2.89	13.33	4.5×3×2.5	74.0	9.86	26.0	3.45	Inguinal
2	16.8	10.0	3.5×2.5×1.5	74.6	7.46	25.4	2.54	17.2	4.5×3×2.5	73.1	12.56	26.9	4.64	Inguinal
3	18.1	10.0	3.25×2.5×1.5	63.0	6.3	37.0	3.7	12.6	4×2.5×1.5	71.6	9.01	28.4	3.59	Inguinal
4	13.6	5.7	3×2×1.5	64.7	3.68	26.3	2.02	13.55	4×2.75×2.5	70.6	9.56	29.4	3.99	Insulinal
5	8.2	2.5	1.8×1×1	53.1	1.32	46.9	1.28	3.5	3×1.5×1	58.7	2.05	41.3	1.45	Inguinal
6	9.1	7.7	3×2×1.5	64.5	4.96	35.5	2.74	13.7	3.5×2.75×2	67.5	9.25	32.5	4.45	Inguinal
7	6.4	7.0	2.5×2×1.5	74.3	5.2	25.7	1.8	10.0	5×2.5×2	71.4	7.14	28.6	2.86	Abdominal
8	6.8	6.6	2.75×2×1.5	66.6	4.4	33.3	2.2	11.3	3.5×2.5×2	70.0	7.91	20.0	3.39	Abdominal
9	16.3	5.2	2.5×1.5×1.5	69.7	3.63	30.3	1.57	10.5	3.5×2.5×2	72.5	7.61	27.5	2.89	Abdominal
10	21.8	14.1	2×1.5×1	56.8	8.01	43.27	6.09	20.0	4×3.5×3	67.3	13.4	32.7	6.5	Abdominal
11	25.4	16.2	3.5×2×1.5	71.4	11.41	29.6	4.79	20.0	4×3.5×3	71.0	14.2	29.0	5.8	Abdominal

another hermaphrodite ground squirrel, which was untreated and which served as a control, the seminiferous tubules lacked lumens but possessed many spermatogonia and occasionally primary spermatocytes. While one does not know whether the treated ovotestis contained spermatozoa before the injection, the presumptive evidence is strong that injection of serum from pregnant mares caused the production of spermatozoa in the ground squirrel (Wells, Wells and Moore). Moore found that mare serum failed to induce formation of spermatozoa in young rats, but Cole, Guilbert and Goss found that the number of spermatocytes was increased in the testes of young rats so treated.

In this study, the right testis of each of 3 adult dogs was elevated to the abdomen, and after the gonad had been there for three months injections of pregnant mare serum were instituted to note any effects on the testis. One hundred and fifty rat units was injected subcutaneously into the flank every other day for a period of seventeen days (1,350 units). The pregnant mare serum was obtained from an eight months pregnant mare at the University Farm School, St. Paul, Minn. The serum was kept sterile and standardized, spayed virgin rats about 160 Gm. in weight being used, so that 1 cc. of the injected serum was equivalent to 150 rat units. On the eighteenth day, the right testis and the left (control) testis were removed. The right testis in every case was embedded in scar tissue and had not descended into the scrotum. It was smaller in size and weight than the scrotal testis.

Right Testis

Dog	Weight, Kg.	Size, Cm.	Weight, Gm.
1	28	3½x2 x1⅓	16.2
2	24	2 x1½x1	14.1
3	18	2½x1½x1½	5.2

Left Testis

Dog	Weight, Kg.	Size, Cm.	Weight, Gm.
1	..	4½x3 x2½	18.3
2	..	4 x3½x3	20.0
3	..	3½x2½x2	10.5

When the testes had been measured and weighed, sections were made and stained with hematoxylin and eosin. The microscopic appearance of the cryptorchid testis was interesting (fig. 4). It was surprising how closely it approached the structure of the normal gland. Tubular degeneration was slight. The interstitial tissue showed little if any increase, and germinal epithelium with spermatozoa was present in all 3 cases. Unfortunately, material for biopsy was not obtained before the injection therapy was begun, but spermatozoa were never seen histologically in testes which had been elevated to the abdomen for three months.

A similar study was carried out with 6 other dogs, weighing from 15 to 22 Kg. The right testis was elevated to the abdomen, and after a two week period of healing 150 rat units of the same pregnant mare serum was injected subcutaneously into the flank weekly for a period of six months. At the end of that time the dog was castrated, and the abdominal and the scrotal testis were examined. Histologically, the abdominal glands of 3 dogs showed fairly normal germinal epithelium; in 1 there were areas of degeneration, and in the other 2 there was

definite degeneration. In my experience, when the testis of an adult dog has been elevated to the abdomen for six months, it always shows degenerative changes (control).

The results of these studies are important, for here is a substance that will maintain the germinal epithelium in spite of an aberrant posi-

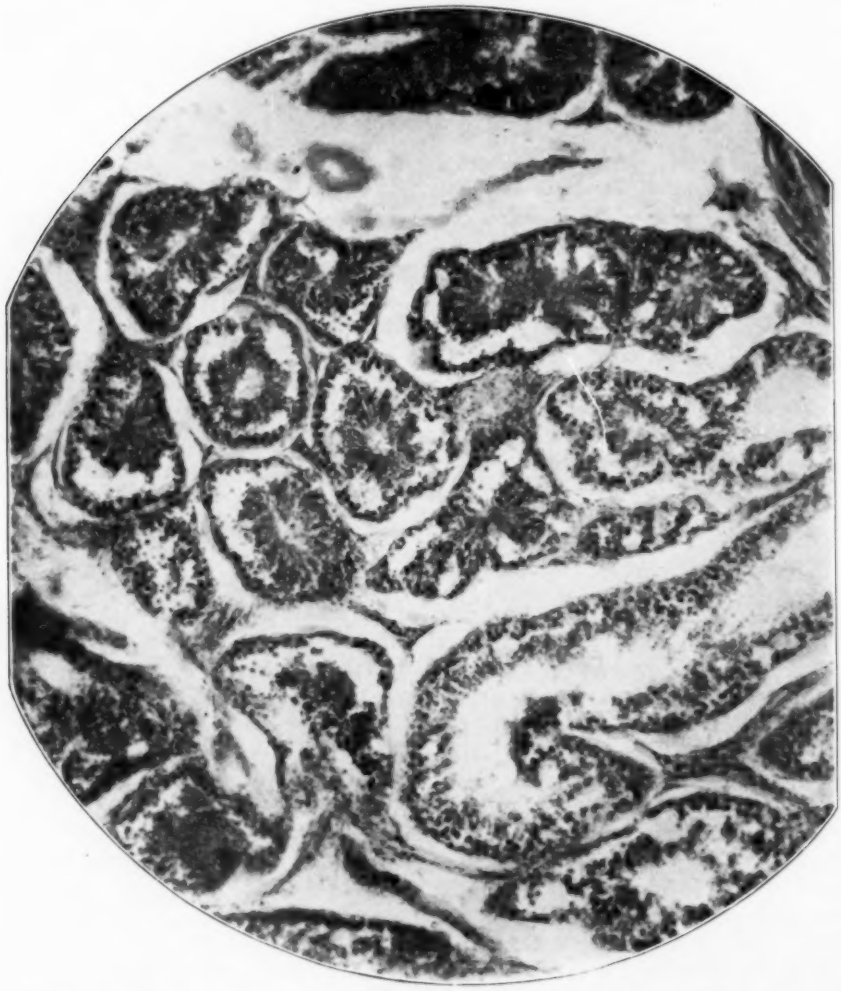

Fig. 4.—Section of an experimentally produced undescended testis of a dog treated with serum from a pregnant mare. Note that the tubules have mature germinal epithelium; spermatozoa are present in most of the tubules. The degree of maturity closely approaches that of a normal descended testis.

tion of the gonad. The question arises as to which is more important: the scrotal (thermoregulatory) or the gonadotropic influences in maintaining the normal testicular function. The importance of the thermoregulatory mechanism of the scrotum in relation to spermatogenesis is

well known from the work of Moore and Wangensteen. The reason why most mammalian testes are susceptible to degeneration caused by their own body heat is unknown. In birds, with a higher body temperature than mammals and with abdominal testes, this thermoregulatory mechanism does not hold. Similarly, in some mammals, such as the whale, elephant and rhinoceros, which do not have scrotums, spermatogenesis is compatible with an intra-abdominal position of the gonad. Moore has suggested that in the latter there may be a correlation between the absence of a scrotum and a lower or less constant body temperature. It may be also that in animals with functional intra-abdominal testes the pituitary gland is more active, regulating the spermatogenic mechanism without benefit of a scrotum. At least the work of Wells and this study would suggest that in certain animals gonadotropic substances may keep the histologic character of the testis normal without the thermoregulatory influence of the scrotum. This might be a partial explanation of the instances of fertility in patients with bilateral cryptorchidism. The final answer, however, awaits further investigation.

8. *Effect of Bringing the Naturally Undescended Testis into the Scrotum.*—It is important to know whether undescended testes when brought into the scrotum will develop normally. In fact, the chief reason for doing an orchiopexy is the hope that maturity will ensue as a result of scrotal position. Most surgeons have been more interested in the cosmetic than in the functional result of operations on the retained gonad. The following results have been noted when the naturally undescended testis has been brought into the scrotum, in man and in animals:

(*a*) Dog. In 1933-1934, 4 adult cryptorchid dogs, weighing 7.5 to 11.15 Kg., were observed in the experimental laboratory. One of these dogs may have been an incomplete castrate; the others had left inguinal testes. With the dogs under pentobarbital sodium anesthesia, both the descended and the undescended testis of each animal were exposed and measured, aseptic precautions being used. After material for biopsy had been taken the undescended testis was anchored in the scrotum. The descended or control gonad was replaced in the scrotum. Three months later the dogs were castrated, and the testes were again measured. In every instance the undescended testis, which had been placed in the scrotum, was smaller than before operation. Microscopic sections of all gonads were made and stained with hematoxylin and eosin. Histologically there was little difference between the biopsy material taken before and that taken after orchiopexy. The previously ectopic organ still had an atrophic appearance. No spermatogenesis was seen. The microscopic sections of two of the descended testes were normal except for some evidence of disorganization even after three months. This emphasizes that great care must be exercised in handling the testis at operation (table 5).

TABLE 5.—*Effect of Scrotal Fixation on the Naturally Undescended Testes of Adult Dogs*

Dog	Weight, Kg.	Age	Descended Testis				Undescended Testis			
			Gross, Before	Microscopic, Before	Gross, After	Microscopic, After	Gross, Before	Microscopic, Before	Gross, After	Microscopic, After
1	7.5	Adult	.....	Normal	Thickened capsule; 1.5×0.5×0.5 cm.	Some degeneration, occasional sperm in tubules	1×0.25×0.25 cm. (left inguinal)	Atrophic; no sperm; outline tubules; 1-2 cells on basement membrane	1×0.25×9.25 cm., thickened capsule	Same; more débris in lumens of tubules
2	11.5	Adult	2.5×2×2 cm.	.....	.....	Tubules full of large dark cells; sperm present; slight disorganization	2.5×2×1.5 cm. (left inguinal)	Very atrophic no sperm; interstitial hypertrophy very prominent	2×1.5×1.5 cm.; thickened capsule fibrous	Same as before
3	10.0	Adult, over 2 yr.	3.5×2×2 cm.	Slight disorganization; sperm present	3.5×2×2 cm.; capsules slightly thickened	Same as before	Left inguinal	.....	2×1.5×1 cm.	Very atrophic hyalinized interstitial tissue; no sperm
4	9.5	Adult	.....	.....	3×2×1.5 cm. capsules slightly thickened	Tubules full of large dark cells; sperm present; very little interstitial tissue	Right inguinal; vas deferens ended in nubbin of tissue about 1.5×1 cm.	Very atrophic; tubular structure (epididymis ?); much connective tissue; no definite testicular tissue	Small fibrous mass	Lymphocytic infiltration; indefinite tubular structure; incomplete castrate ?

Two factors may have influenced these results: 1. The dogs were full grown and the germinal epithelium may have been too atrophic to regenerate. 2. In none of the dogs did the surgically treated testis remain low in the scrotum; instead, it attained a high position near the base of the penis.

(*b*) Pig. While the results of operation on dogs were disappointing, better results have been obtained from performing orchiopexy on pigs.

Wangensteen reported the results of orchiopexy in 3 young pigs with congenital inguinal testes which had the microscopic appearance of prepubertal gonads. Two, four and ten months after operation respectively, the animals were killed and biopsies of the surgically treated testes revealed mature germinal epithelium with spermatozoa. In other pigs, in which the abdominal testis was anchored beneath the skin of the groin, mature germinal epithelium was not observed. Since spermatogenesis has never been observed in sections of the undescended testis of the adult boar in this laboratory, it cannot be denied that the germinal epithelium is improved by fixation of the testes in the scrotum.

These results are the same as those previously observed by Moore, Wangensteen and others when in the dog and guinea pig the testis previously placed in the abdomen has been replaced in the scrotum and seen to regenerate. However, experiments with naturally cryptorchid pigs give more conclusive proof of the value of orchiopexy, because the results are free from objections which might be raised against the use of the animals in which cryptorchidism had been produced experimentally.

In comparing the results obtained from orchiopexy in natural cryptorchids with those of the same operation in the experimental variety, it is to be noted that the degree of maturity obtained in the former is never as great as that occurring in the latter (Wangensteen).

(*c*) Man. At the University Hospitals for the past few years, smears and biopsies have been made of material from undescended testes at the time of orchiopexy. The ages of the patients varied from 9 to 26 years. Microscopic sections from 17 and smears from 8 of these did not disclose spermatozoa. When the scrotum was detached from the thigh, usually six months after the orchiopexy, a small amount of material for biopsy was again taken from the periphery of the testis. Histologic study of the material from 4 of these patients (15 to 24 years of age) showed no spermatozoa. The germinal epithelium, while occasionally improved, never showed complete maturation. However, a case reported by Wangensteen is of particular importance:

> The patient was first seen at the age of 20 years. He had inguinal testes, for which he was treated by orchiopexy, first on the right and then on the left.

Biopsy at operation showed tubules with atrophic epithelium and no spermatozoa. Sections of the testes removed at the time of detachment of the scrotum from the thigh four and six months later revealed an improved but not mature germinal epithelium. No spermatozoa were seen. Sixteen months after the latter operation the patient was accidentally killed.

At postmortem examination the testes were low in the scrotum and were about two thirds the normal size. The histologic appearance of the right testis was nearly normal. The left testis, while exhibiting some normal spermatogenesis, showed more atrophy than maturation. Examination of the semen one week before death had revealed only occasional spermatozoa. This is the only clinical case recorded in available literature which definitely proves that the germinal epithelium of the human undescended testis may improve after orchiopexy.

Possibly in most of my cases histologic examination was made too early to permit determination of the degree of maturity which might finally be attained. Access to the whole gland, as in the case of the castrated animal, for multiple smears and sections might alter the results obtained when smears and sections of the undescended testes are studied for signs of maturation. Moreover, the histologic effect of orchiopexy in Wangensteen's case and the undoubted examples of fertility in human cryptorchids cast further doubt on these negative results. Finally, since potential fertility may persist into adult life in lower animals with undescended testes, the sum of the evidence tends to indicate that nearly all patients with undescended testes should be subjected to orchiopexy.

9. *Effect on the Naturally Undescended Testis of the Use of Various Preparations of Gonadotropic Substance from the Urine of Pregnant Women and from the Anterior Lobe of the Pituitary.*—(*a*) Dog. Antuitrin-S [3] was injected into 2 adult dogs, weighing 10 and 12.5 Kg., respectively, with congenital unilateral inguinal testis. One hundred rat units (1 cc.) was injected daily subcutaneously until 3,000 units had been given. Descent was not observed in either case. One month later the testes were removed.

Each undescended testis was embedded in fibrous connective tissue and was smaller than its normally located fellow. Microscopic section failed to reveal any spermatozoa, and the organs had the usual atrophic appearance. Smears of the cut surfaces failed to show spermatozoa. Studies of the relative amount of interstitial tissue and of the size of the tubules could not be made before and after treatment, since removal of material for biopsy before treatment would have altered the appearance of the testes. Unfortunately, the pituitary glands of these animals were not studied (fig. 5).

The doses of antuitrin-S were the same as those used for man. Considering the difference in body weight, this was an excessive dose.

3. Antuitrin-S (Parke, Davis & Co.) is a gonadotropic substance extracted from urine of pregnant women.

This may have influenced the results, but the age of the dogs and the fibrous adhesions surrounding the testes were probably the more important factors.

(*b*) Man. For the past four years, at the University Hospitals, undescended testes in some cases have been treated by the administration of

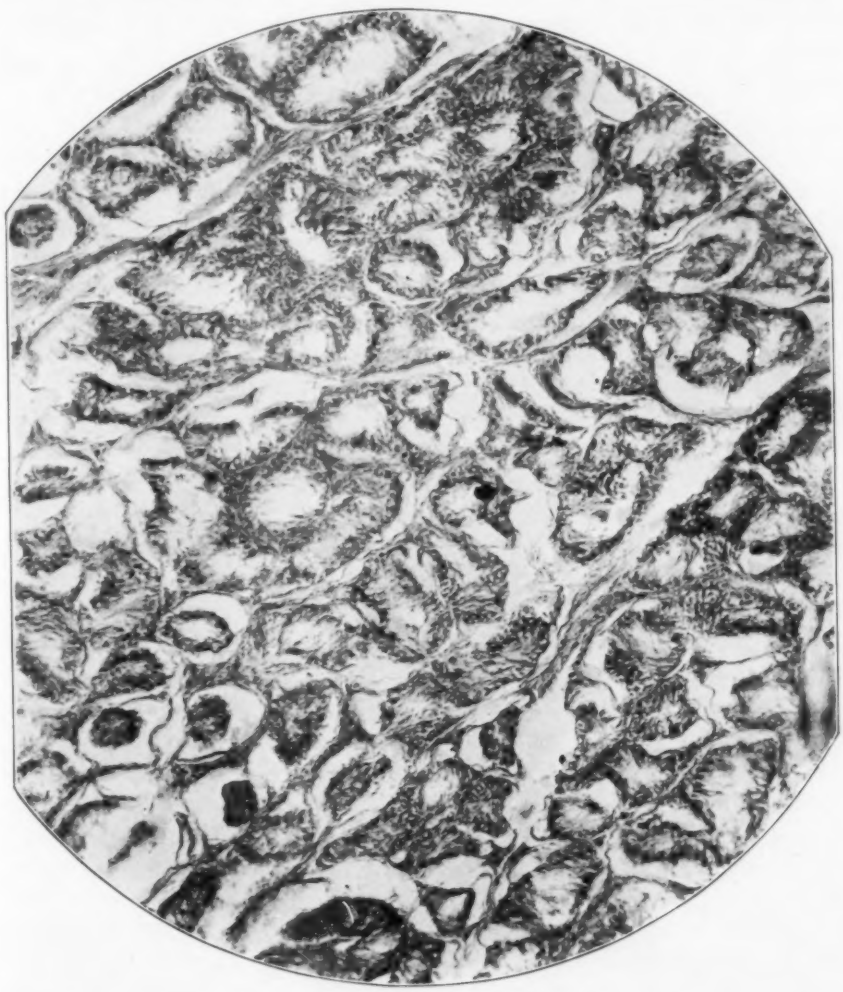

Fig. 5.—Congenitally undescended testis (× 700) of an adult dog treated with antuitrin-S (3,000 units). The usual degenerated appearance still persists. Compare with figure 1.

gonadotropic substances. Schapiro in 1930 reported having obtained genital growth and testicular descent in boys and young men with hypogenitalism and cryptorchidism by the use of the gonadotropic substance from the urine of pregnant women. Since then the literature has con-

tained reports of several series of cases in which undescended testis was treated by the use of this material. Thompson and his associates and also Cramer have recently summarized the results of most of the investigators; in over 70 per cent of cases descent of the retained gonad has occurred. How critically some of the cases were observed may be questioned when in one series the testis was reported to have descended within three hours after treatment (Harris). About half of the patients showed signs of hypopituitarism or adiposogenitodystrophy and received other therapy besides that employing gonadotropic substances (e. g., treatment with thyroid extract or a dietary regimen). From a summary of published data, the original position of the gonad successfully brought into the scrotum by the gonadotropic substance obtained from the urine of pregnant women was as follows: high scrotal, intra-abdominal and inguinal, in the order named (Thompson and others).

Kunstadter and Robins, Schapiro, and Goldman and Stern concluded that the administration of the gonadotropic substance obtained from the urine of pregnant women is indicated in hypopituitarism of the male characterized by genital underdevelopment. However, the clinical diagnosis of pituitary or other endocrine dyscrasia is always subject to considerable variation in interpretation. Hess, Kunstadter and Saphir expressed the opinion that if cryptorchidism could be studied with more objective criteria a more rational therapy could be instituted. It is known that whenever gonadal function is diminished or absent, as in adult hypogonadism, castration or the menopause (Evans, Engle and Smith), there is excessive excretion of gonadotropic substance, presumably of pituitary origin. Katzman and Doisy showed that the urine of normal children contains little or no gonadotropic substance. Hess and his co-workers reasoned that since in castrated persons or in cryptorchid boys the gonadotrpoic hormone is presumably of pituitary origin, it seems logical to conclude that the presence of gonadotropic substance in the urine of cryptorchids indicates that the anterior lobe of the pituitary gland is active in gonadotropic function. The appearance of the gonadotropic substance in the urine may be due to insufficient activity of the gonad, which failed to modify the hormone or to remove it from the blood. On the other hand, the occurrence of cryptorchidism with absence of gonadotropic substance from the urine may be interpreted to mean either that there is primary pituitary dysfunction or that the undescended testes are functionally active or that at least one of them is.

Accordingly, Hess and his associates determined in a semiquantitative manner the excretion of gonadotropic substance in the urine of cryptorchid boys before and after treatment with the gonadotropic substance obtained from the urine of pregnant women. Nine of their 13 patients with cryptorchidism responded to the use of the gonadotropic substance by descent of the testis and disappearance of gonadotropic

substance from the urine. They concluded that in the absence of mechanical obstruction to descent the best results from the use of this gonadotropic substance are obtained in those cases of undescended testis in which gonadotropic substance is present in the urine but disappears after treatment.

Hardy, Bigler and Scott reported results in one of the largest series of cryptorchids treated with gonadotropic substances that have been recorded to date. In one group, 32 boys with 40 undescended testes were treated with an extract of the anterior lobe of the pituitary gland which contained the gonadotropic principle. In 26 cases the testicles remained unchanged in location, in 4 there was partial descent, and in 10, or 25 per cent, there was complete descent. After treatment was discontinued, however, only 7, or 18 per cent, of the testes remained descended. In another group, gonadotropic substance from the urine of pregnant women (antuitrin-S) was used in the treatment of 23 patients with 31 undescended testicles. No change was observed in the location of 12 testicles; 4 descended partially, and 15, or 48 per cent, descended completely. However, only 14 testes, or 45 per cent, remained descended. Both extracts were used in the treatment of 16 boys with 20 undescended testicles. In 9 cases there was no change, in 2 descent occurred, and in 9, or 45 per cent, there was complete descent, which was permament in 5, or 25 per cent. They found that descent of the testicle usually begins to take place before 4,000 rat units of gonadotropic substance has been given.

Undoubtedly, in the literature more prominence has been given to successes than to failures. Few contraindications to therapeutic use of gonadotropic substances are recognized, and the therapy is too recent to permit investigation of the possibility of late complications. Thompson and others obtained descent of 4 inguinally retained testes in 21 instances of cryptorchidism (19 per cent). Mimpriss, who obtained descent in only 6 of 20 patients with undescended testis who were so treated, concluded that the gonadotropic substance from the urine of pregnant women should be used chiefly for patients with bilateral cryptorchidism and subnormal genital development. Cabot referred to the possibility of late atrophy of the testes, and Cole produced atrophy of the tubules of the testes by high doses. Goldman and Stern commented on the possible development of precocious sexual maturity and for this reason gave 9 years as the earliest age at which treatment with gonadotropic substances should be started. In this clinic also there is some hesitancy in using the gonadotropic substance from the urine of pregnant women for very young children, but Dorff and also Aberle and Jenkins reported using it for children about 3 years of age with no untoward results. Geschickter and his associates found that young male monkeys given the gonadotropic substance from the urine of pregnant

women presented hypertrophy of the prostate and enlargement of the breasts. However, from a survey of the available literature and the experience at this clinic, the danger of most such complications would seem more theoretic than actual.

The results from the use of gonadotropic substances in the treatment of retained testes observed at the University Hospitals will be summarized now. Four products have been tried: antuitrin-S (Parke Davis & Co.), follutein (Squibb), prephysin (Chappel) and A. P. L. (Ayerst).[4] The last three products have been used in only a few cases.

Antuitrin-S. It has been my practice to inject 1 cc. (100 rat units) of antuitrin-S daily into the subcutaneous tissue of the thighs for thirty days (3,000 units). If no results are obtained before this time, the patient is observed every month for three months and then every three months. Some of the cases in which no results were obtained have been followed for two years.

Thirty patients with 36 undescended testes have been treated to date with antruitin-S in this clinic. The ages of the patients varied from 4 to 24 years. The testes were bilaterally retained in 6 instances. Two of the patients with bilateral cryptorchidism also had hypospadias; in a third patient with bilateral cryptorchidism and in a patient with testes inguinally retained there was a suggestion of Fröhlich's syndrome. In 5 patients the retained testes responded to the treatment by degrees of descent into the scrotum. The descent in 3 was complete; the descent in the other 2 was only to a high scrotal position. The latter patients were older, and both later submitted to orchiopexy. One of these patients received a total of 6,000 units over a period of two months. It is interesting that when the patient later submitted to orchiopexy no spermatozoa were seen in either the biopsy or the examination of the smear. Also, the microscopic section of the testis showed the usual atrophic appearance.

No untoward results following the use of antuitrin-S in this clinic have been observed over a period of two years. Three patients had suprapubic edema, which disappeared after treatment. Another patient complained of swelling in the left breast, which clinically was thought to be fibrous mastitis. In none was there a demonstrable increase in the size of the penis. The testes of the successfully treated patients often enlarged; I could not be sure that there was any change in size of the testes of the unsuccessfully treated patients. One boy showed a red and slightly edematous appearance of the scrotum when 2,000 units of antuitrin-S had been administered. In none of the patients was there premature appearance or increase in the amount of pubic, axillary or facial hair. Five patients noticed increased frequency of erections.

Follutein. Two patients, aged 21 and 23 years, were treated with follutein for undescended testes. One patient had bilateral inguinal testis; the other had the right testis inguinally arrested. One cubic centimeter (125 units) of follutein was injected into the subcutaneous tissue of the thigh daily for ten days (1,250 units). No improvement was noted; the patients were observed for a period of one year.

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4. Antuitrin-S and follutein are preparations of the gonadotropic substance from the urine of pregnant women. Prephysin is an extract of the anterior lobe of the pituitary gland. A. P. L. contains gonadotropic substance derived from the placenta.

Prephysin. Three patients, aged 2, 7 and 11 years, were treated with prephysin. All three had unilateral inguinally retained testis. The two younger boys were brothers. Prephysin contains the follicle-stimulating principle of the pituitary gland, including small amounts of luteinizing factor. It differs from antuitrin-S and follutein in that it is extracted from the pituitary gland itself and not from the urine of pregnant women. Each boy was given 2 cc. of prephysin (1 cc. is equivalent to 25 units), 0.5 cc. being injected into the subcutaneous tissue of a thigh daily for four days. No descent of the testis was observed in any of these boys over a period of nine months.

A. P. L. ("Anterior Pituitary-Like Substance"). To date 4 patients have been treated with this substance, which is extracted from placental tissue. The special strength solution, 500 units per cubic centimeter, has been used in doses of 0.5 cc. every other day until fifteen injections have been given. Three patients with unilateral inguinal testes have been treated with this substance and observed less than five months. No beneficial results have been noted to date. However, in the fourth patient, a boy 9 years old, with bilateral inguinal testes, complete descent of both testes occurred after the ninth injection.

Thus, in summary, one may state that of 36 patients with undescended testes who were treated with gonadotropic substances and followed six months or longer, degrees of descent were noted in 6 (16 per cent). In 4, descent was complete. It is possible that the dosage and period of injection of gonadotropic substances in these cases were not adequate, but these factors are comparable to those reported in the successfully treated cases in the literature (Hardy, Bigler and Scott; Cramer).

Evaluation of the Treatment of Ectopic Testis with Gonadotropic Substance.—Rubenstein in the following statement has summarized the current concept regarding the use of gonadotropic substances in the treatment of undescended testis. The water-soluble fraction of the urine of pregnant women seems to produce testicular descent only if the pituitary gland is underdeveloped from the standpoint of the production of the gonadotropic hormone. The injection of this fraction then leads predominately to a stimulation of the interstitial cells of the testicle, and if a mechanical block does not exist, may result in descent.

Nearly all the patients with cryptorchidism who have been operated on at the University Hospitals have shown evidence of mechanical arrest of testicular descent. The testes were often lodged in pockets or bound down by adhesions to such an extent that it was with great difficulty that they were freed or the spermatic cord lengthened sufficiently by loosening adhesions. It is almost inconceivable how one could bring such testes into the scrotum without surgical measures. MacCollum pointed out that it is incongruous to suppose that at some time this fibrous tissue will disappear and allow the testicle "to drop like a plummet" into the scrotum. In my series, 5 patients with undescended testes who had been treated with antuitrin-S (total 3,000 units for each except a patient who was given 6,000 units) submitted to operation

three to six months later. The same degree of fibrous adhesion and mechanical arrest seemed to be present in these as in patients who had not been treated with gonadotropic substance prior to operation. The mechanical obstruction to spontaneous or induced testicular descent as revealed by operation seems adequate explanation of the failure of therapy employing the aforementioned gonadotropic factor.

One wonders if many of the successful results reported in the literature as following endocrine therapy were not obtained in cases of physiologic ectopy and not in cases of true undescended testis. It may be that the gonadotropic substance obtained from the urine of pregnant women is valuable in the treatment of physiologic ectopy, but it should be remembered that in such cases the testes often descend spontaneously. It is not to be inferred that I believe that all the reported cases of retained testes that have descended after a course of endocrine therapy were cases of physiologic ectopy. However, because of the results obtained with this therapy at this clinic and because of the existence of mechanical causes for testicular arrest in most of the cases in which operation was performed, it is believed that endocrine imbalance alone does not fully explain the cause or give a rational basis for treatment in all cases of true testicular maldescent.

There can be no doubt that in some cases of cryptorchidism gonadotropic substances will cause descent of the testis into the scrotum; in others endocrine therapy is of no value and only surgical treatment will remedy the aberrant position of the gonad. In a third group, testicular descent or size may be enhanced by the preoperative or postoperative use of glandular substances. Just what percentages of undescended testes fall in the aforementioned classifications is unknown. However, a method that gives the patient any chance of avoiding a surgical operation certainly merits trial; hence, the use of endocrine therapy at least as a preliminary form of treatment seems indicated.

Suggested Plan of Treatment for Undescended Testis.—It is known from the experiments of Moore and Wangensteen that the testis must be in the scrotum before spermatogenesis occurs, or degenerative changes will set in. Puberty in the male occurs between the ages of 13 and 15 years, without regard to race, climate or individual differences (Spangaro), the extremes being 9 (Scammon) and 18 years (Crampton). Therefore, treatment of the congenitally retained gland may be deferred until the patient is 9 to 11 years old. If no complications are present, there is no objection to operating on a patient with retained testis at any earlier age, but it is unnecessary. The presence of a large associated hernia may necessitate earlier surgical intervention, since an undescended testis precludes the use of a truss and injection of a sclerosing solution in the treatment of inguinal hernia. It is the practice at the University Hospitals to suggest first a trial of the gonadotropic

substance obtained from the urine of pregnant women in all uncomplicated cases of undescended testes before surgical procedures are undertaken. Possibly the determination of gonadotropic substance in the urine before treatment (Hess and others) will aid in the selection of patients for this treatment. It would be of practical value to know before treatment whether there are mechanical causes for the testicular maldescent, but unfortunately no way to determine this is known. There are various methods of administering endocrine therapy. While the available gonadotropic substances are well standardized, the doses and intervals of injection prescribed by various authors are rather empiric. At this clinic the methods of treatment outlined in a foregoing section are still followed, except that greater doses are given in some instances, as well as subsequent courses of injections, at two to three month intervals, if the patient is under 9 years of age. I have had no experience with extremely large doses of gonadotropic substances in the treatment of cryptorchids at this clinic, as the cost is prohibitive. If after six months of observation no results have been observed from endocrine therapy, surgical treatment of the undescended testis is advised if the patient is 9 years old or older.

In résumé the following points should be reemphasized: Treatment of the retained gonad may be deferred until the patient is 9 to 11 years old. Reports in the literature on cryptorchids treated by gonadotropic "hormones" reveal that in as high as 70 per cent there is descent of the testes into the scrotum. With the hope that the case may be a favorable one, a course of treatment with the gonadotropic substance obtained from the urine of pregnant women may be tried first. This form of therapy has not been as efficacious in the cryptorchids treated to date at this clinic, degrees of descent being obtained in only 16 per cent of the patients so treated. No untoward effects resulting from such therapy have been observed.

For reasons mentioned elsewhere, it is believed that endocrine imbalance alone does not fully explain the cause or give a rational basis for treatment in all cases of true testicular maldescent. However, a gonadotropic substance should be given at least a preliminary trial in the treatment of undescended testis, and if no results are obtained an orchiopexy should be performed.

V. SUMMARY

The causes of failure of the testes to descend are unknown, but endocrine imbalance is probably one of these factors. Undescended testes do not differ grossly or histologically from the normal up to puberty, but after this they undergo degenerative changes. Just how long the undescended human testis remains capable of function is unknown, but there are undoubtedly isolated cases in which spermato-

genesis has persisted into adult life. In this study, smears of cut sections of abdominal testes occurring naturally in adult pigs not infrequently showed spermatozoa. The superiority of the smear over the microscopic section of the testis in determining the presence of spermatozoa has been shown.

From a review of the literature, it seems established that most undescended testes have an internal secretion and occasionally may possess an external secretion sufficient for potential, if not absolute, fertility. It is estimated that 10 per cent of untreated human cryptorchids remain fertile.

It has been proved clinically that as high as 82 per cent of those treated by orchiopexy have active spermatozoa in the semen. Placing the slightly atrophic or immature retained testis of man or of the pig into the scrotum has been shown experimentally to permit the germinal epithelium to mature. The degree of maturity after orchiopexy for natural failure of descent is never as great as that seen after the same treatment in the case of experimentally produced cryptorchidism. However, clinically and experimentally the value of orchiopexy for promoting maturation of the germinal epithelium has been demonstrated beyond doubt.

Various preparations of the gonadotropic substance have been used clinically and experimentally at this clinic to cause descent of the testes into the scrotum. The indications for and limitations of such therapy are as yet in an empiric stage. Proof is lacking to date that this form of therapy will cause germinal maturation in the naturally cryptorchid testis. That serum from pregnant mares may maintain the normal histologic appearance of the testis in spite of an aberrant position of the gland has been suggested from experimental investigations. In this study, the hypophyses of 5 pigs with naturally occurring retained gonads failed to show any castration cells. The gonadal-pituitary relation is probably more labile than is generally believed. The relative importance in the function of the testis of the scrotal (thermoregulatory) hormonal balance has not been established.

Judging from the number of spermatozoa in the ejaculated semen as well as from the histologic appearance of the undescended testis after orchiopexy, such organs probably never attain an entirely normal functional capacity. Whether the potential function of the ectopic testis is inherently smaller than that of the descended gland is unknown. Histologic examination up to the time of puberty and the results of tissue culture fail to show any positive proof of congenital imperfection. Most of the imperfections become apparent at puberty, probably as the result of the influences of hormonal and of extrinsic anatomic factors arising at that time.

The following findings also seem established:

1. Failure of the testis to descend should not be considered a precancerous condition.

2. Treatment of the undescended testis may be deferred until the ninth to eleventh years. Treatment with a gonadotropic substance may be tried first, but if no results are apparent within six months orchiopexy should be performed.

3. Obstruction to the pathways for seminal transmission does not result in permanent testicular degeneration.

4. In the dog with experimentally produced cryptorchidism the increase in the interstitial tissue of the testis is relative and not absolute.

5. The observations on natural cryptorchids parallel in general those on animals in which cryptorchidism was experimentally produced.

VI. CONCLUSION

The undescended testis, either untreated or after orchiopexy, never attains the full functional capacity of the normally descended organ as far as the production of spermatozoa is concerned. However, the value of orchiopexy in promoting the development of the undescended testis has been proved clinically and experimentally in both natural and experimentally produced cryptorchids.

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ROUTES OF ABSORPTION IN TOTAL URETERAL OBSTRUCTION

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A previous contribution [1] on the routes of absorption in the presence of hydronephrosis, based on experiments with molecular dyes and colloidal preparations, demonstrated that there are two routes of absorption, lymphatic and tubular. In the previous investigation, at the onset of complete ureteral obstruction there ensued for about two or three days a purely lymphatic absorption from the walls of the renal pelvis and the ureter. After approximately the third day a tubular absorption began, and this continued more actively than the lymphatic absorption. It was noted that the distal convoluted tubules of the peripheral layer of glomeruli were the first to assume this function, and as pressure atrophy progressed the subjacent tubule layers, seriatim, continued the process. The cells of the convoluted tubules by thus absorbing the mediums demonstrated a slightly altered function and one of definite significance in renal pathology.

Throughout the investigation care was taken not to strain the pelvic capacity but to inject an amount of dye less than the pelvic contents as shown by aspiration. As a result of misjudgment of the capacity in 2 instances, overdistention occurred, and as a result of pyelovenous back flow, dissemination of the dye into the general system was observed, reticuloendothelial cells of the liver and spleen showing obvious presence of the dye. Apart from these 2 instances no evidence of absorption into the general system was found throughout the investigation.

As it was felt that this failure was probably due to the comparatively large molecular values of the mediums employed, it was decided to continue investigation with other agents and to observe whenever possible the actual process of absorption in the living tissues.

From the Wilkie Surgical Research Laboratory, University of Edinburgh.

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1. Morison, D. M.: Routes of Absorpti n Hydronephrosis: Experimentation with Dyes in the Totally Obstructed Ureter, Brit. J. Urol. **1**:30-45 (March) 1929.

PURPOSE OF THIS STUDY

The following experiments were undertaken:

1. To determine by their elimination from the healthy kidney the rate of absorption from the hydronephrotic sac of agents routinely employed in the estimation of renal function.

2. By similar procedures to those previously adopted to study the routes of lymphatic absorption from the obstructed pelvis.

3. By direct observation of the normal and the obstructed ureter and kidney to determine the rate and routes of lymphatic absorption after intramural and parenchymal injections of dye.

4. By direct observation to note the rate and mode of absorption of dye from the lumen of (*a*) the ureter and (*b*) the renal pelvis.

5. To study the lining epithelium of the upper part of the ureter and the renal pelvis after vital staining.

To obviate unnecessary repetition, the two main operative procedures employed as a preliminary to a number of the group experiments are described here and are briefly referred to subsequently as operation A and operation B (fig. 1).

TECHNIC AND OPERATIVE PROCEDURES

The animals used were rabbits under open ether anesthesia.

Operation A.—Through a midline suprapubic incision, the left ureter was identified at the bladder and divided between ligatures. The wound was closed. The animals were kept thereafter for varying periods as desired, with total obstruction of the left ureter.

Operation B.—On expiration of the desired period of hydronephrosis the animal was again anesthetized with ether, and the suprapubic wound was reopened and continued up to the epigastrium. The abdominal contents were then packed off so as to expose completely the left kidney and its pedicle, together with the entire length of the obstructed ureter.

When it was desired to introduce dye into the ureteral lumen and maintain hydronephrosis in order to observe absorptive changes in the kidney and ureter, the following procedure was carried out:

The lower end of the obstructed ureter was mobilized, and two ligatures were so placed that the upper one was left with a loose single knot and the lower one was tied at once and used for traction. Between the two ligatures the ureter was sufficiently opened to admit an F 4 ureteral catheter; on this the loose upper ligature was sufficiently tightened to prevent leakage of contents. To obviate trauma of the ureteral epithelium the catheter was advanced gently as far as the pelvoureteral level, and aspiration of its contents was done. Particular care was taken in each instance, as before, to introduce a quantity of medium less than the amount of contents aspirated. After the injection the previously tightened ligature was firmly tied on the ureter as the catheter was withdrawn. Measures were taken to preclude any leakage of dye.

RATE OF ABSORPTION FROM THE HYDRONEPHROTIC SAC

Since intravenous pyelographic mediums and dyes are routinely employed for the estimation of renal function, uroselectan B (known in the United States as neo-iopax), phenolsulfonphthalein and indigo carmine suggested themselves.

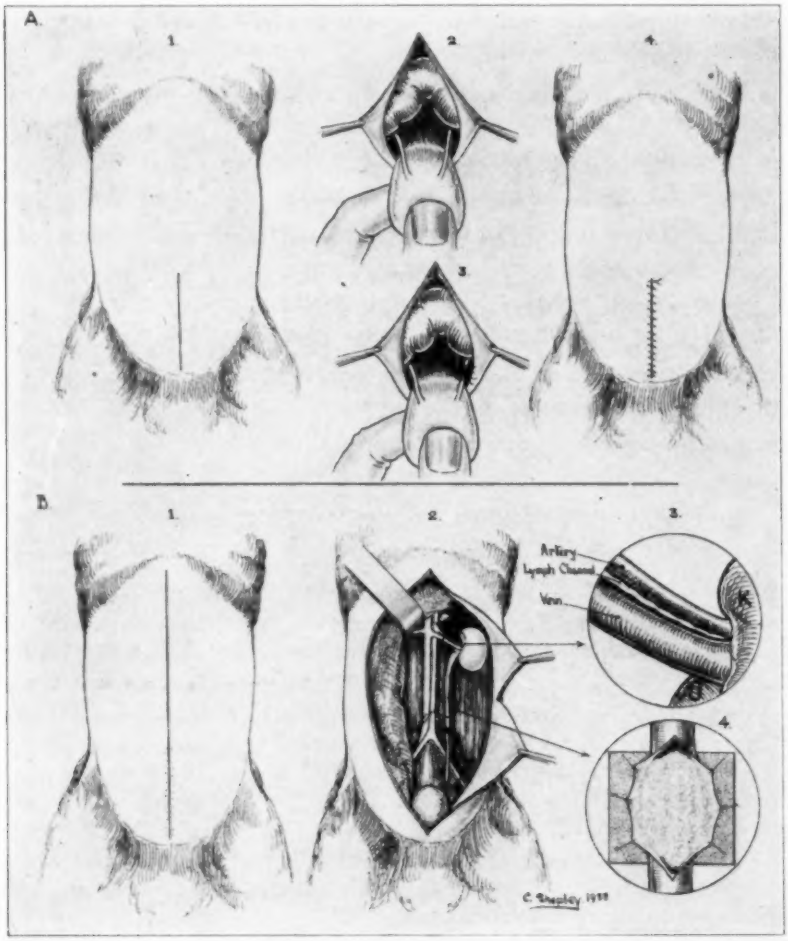

Fig. 1.—Operative procedures: *A*, ligation of the left ureter, showing (*1*) the incision, (*2*) the bladder displaced downward to expose the ureters, (*3*) the left ureter divided between ligatures and (*4*) the wound as closed. *B*, complete exposure of the left kidney and ureter, showing (*1*) the incision, (*2*) the abdominal contents packed off, with exposure of the left kidney and ureter, (*3*) a detail of the renal pedicle, and (*4*) a segment of the ureter prepared for study of the lining epithelium.

Clinical Studies.—A small number of clinical cases of unilateral hydronephrosis was studied by the introduction of uroselectan B into the affected side after partial or total aspiration of the contents. If

ureteral spasm followed withdrawal of the catheter, it was noted by serial roentgen studies that in about thirty minutes after introduction of the opaque medium into the hydronephrotic sac the parenchymal outline of the opposite, healthy kidney began to manifest itself, and presently a definite pyelogram of this side appeared (figs. 2 and 3).

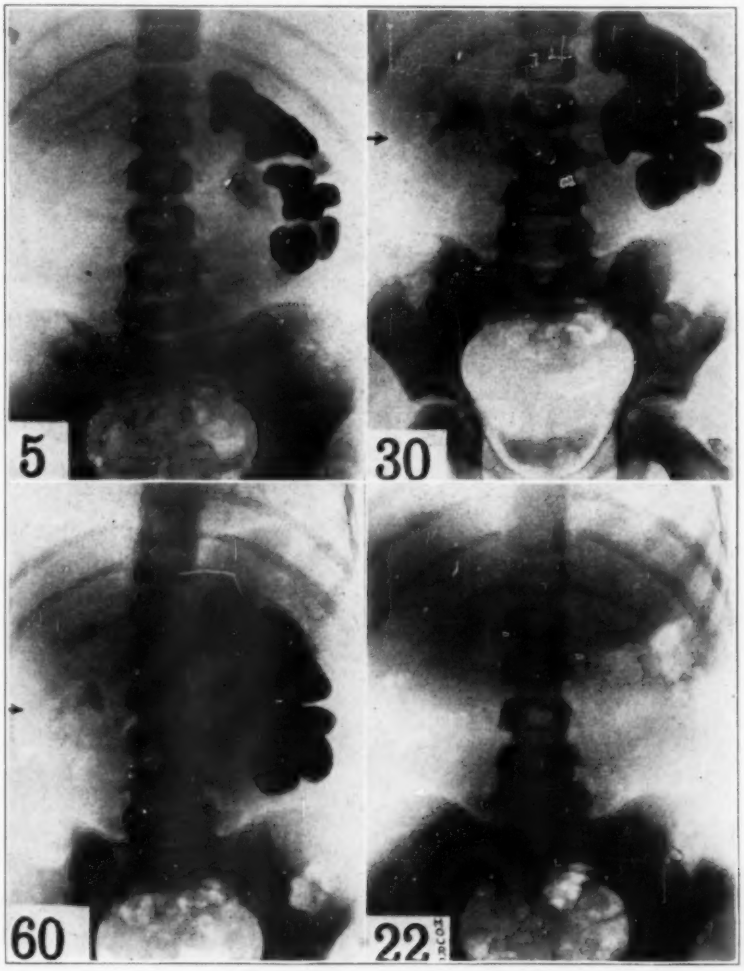

Fig. 2.—Congenital unilateral hydronephrosis. The serial pyelograms were taken five, thirty and sixty minutes and twenty-two hours after introduction of uroselectan B into the hydronephrotic sac. The films taken at thirty and sixty minutes show by reabsorption from the affected side a faint but definite pyelogram of the opposite, healthy kidney.

Experimental Studies.—As it was desired to obtain more detailed data as to the mode of absorption of the opaque medium from the hydro-

nephrotic side into the general system (as proved by its elimination from the opposite, healthy kidney), a series of similar studies was carried out on rabbits at varying periods after total ureteral obstruction. The data obtained were not sufficiently convincing, though similar to those obtained from studies on man. In some instances, however, the cortical

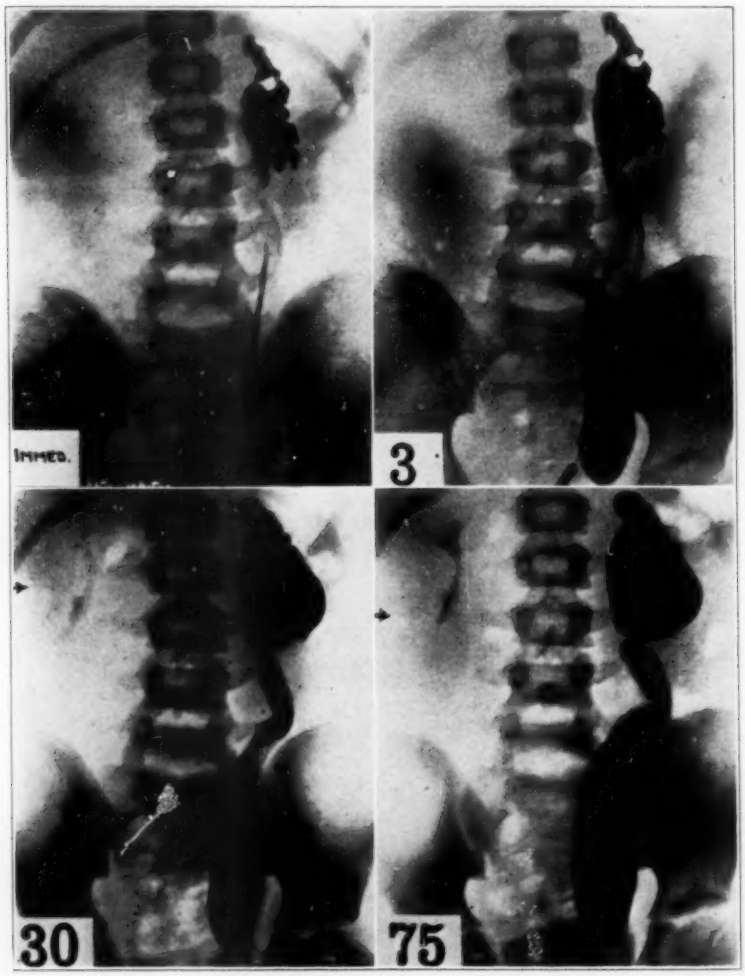

Fig. 3.—Congenital left hydronephrosis with hydroureter. The serial pyelograms were taken immediately and three, thirty and seventy-five minutes after the introduction of uroselectan B into the affected side. In thirty minutes after pelvic and ureteral capacity has been reestablished the pyelogram of the right kidney begins to show the dye.

zone of the hydronephrotic side revealed a radial increased density prior to the appearance of the opaque medium in the bladder from the unobstructed side.

To determine whether absorption took place by way of lymphatic or venous routes, comparative determinations were made on animals both with and without prior interruption of the main lymphatic channels of the renal pedicle. Before, and at intervals during, the period of absorption of the medium from the hydronephrotic side, samples of blood were drawn off from the renal vein and subsequently studied roentgenographically. None of the samples showed any evidence of variation in density.

The findings in relation to indigo carmine and phenolsulfonphthalein were as follows: After injection into the veins of the ear the former dye appeared in the vesical urine in ten minutes and the latter in barely two minutes. When introduced into the hydronephrotic sac, phenolsulfonphthalein usually appeared in the bladder by excretion from the healthy side in about one hour, whereas indigo carmine in most instances did not show for four hours or longer.

The effect of lymphatic interruption at the renal pedicle was tried in a small number of animals. It did not appear to influence in any way the rate of appearance of either of the dyes used. Similarly, the preliminary administration of 20 cc. of physiologic solution of sodium chloride intravenously as well as 20 cc. subcutaneously did not materially alter the time of appearance of these dyes.

ROUTES OF LYMPHATIC ABSORPTION FROM THE OBSTRUCTED PELVIS

As pontamine sky blue is regarded as having an affinity for lymphatics, this dye was employed in a series of animals in a manner similar to that adopted in the original published investigation, in which berlin blue (aniline blue), pelican ink and other medicines were used. The studies revealed no additional information regarding the routes of lymphatic drainage. Tubular absorption was depicted as clearly as with the other dyes.

RATE AND ROUTES OF LYMPHATIC ABSORPTION AFTER INTRAMURAL AND PARENCHYMAL INJECTIONS OF DYE

The work of previous investigators on the lymphatic system has shown that the rate of absorption in certain regions is rapid, particularly from the ovary, the testis and the cervix. Similarly, dyes injected into the superficial aspect of the renal parenchyma around the hilus are quickly absorbed and are soon evident in the main lymphatic channels of the renal pedicle. It was felt, accordingly, that fresh data might be obtained if the process of absorption was carefully watched under the binocular microscope during life.

At the outset, small quantities of pontamine sky blue were injected under binocular control with a fine needle into the ureteral wall at different levels. Ureters that had been obstructed for various periods were studied and compared with the normal ureter. No dramatic evidence of lymphatic absorption could be detected at the time of injection or for two to three hours subsequently, despite continuous observation. Similar procedures applied to the superficial zones of the renal cortex disclosed at times a definite intratubular distribution of dye, the affected tubules taking on the same appearance as in absorption. With such injections the lymph channels of the pedicle showed no dye content. At other times the injected dye entered only the intertubular spaces and graphically showed up, in contrast, the arrangement of the superficial tubules. In these instances, within a space of one or two minutes the pedicle lymphatics disclosed an easily discernible dye content. It has been stated that dye injected into the renal parenchyma near the hilus readily finds its way into the pedicle lymph channels, but the aforementioned tests, which gave similar results, were carried out on the outer border of the kidney, well away from the hilus.

RATE AND MODE OF ABSORPTION OF DYE FROM THE LUMEN OF THE URETER AND THE RENAL PELVIS

(*a*) *Absorption from the Ureteral Lumen.*—Several dyes, i. e., pelican ink, lampblack, janus black, gentian violet and pontamine sky blue, were employed. After repeated experiments, however, it was found that pontamine sky blue in 2 per cent and 5 per cent freshly prepared aqueous solution was the most satisfactory. The dye was introduced into the ureters, which had been totally obstructed for periods varying from a few minutes to four or five weeks.

From the surface no evidence of dye passing along the lymph channels could be detected. As in these experiments the renal changes also were being watched, the animals were killed at periods varying from two to twelve hours after introduction of the dye. After fixation for twenty-four to forty-eight hours the ureters were divided at the renal pelvis, longitudinally opened and pinned out on cork (fig. 4). A gentle stream of water was used to remove any free dye remaining. Microscopic study of the ureters from their mucosal surface usually revealed a mixed grouping of cell types over different areas (fig. 5). There appeared to be a patchy distribution of absorption. Here and there, large flat transitional epithelial cells were present in irregular groups, but most areas showed smaller forms, apparently of a subjacent layer, with relatively larger nuclei and arranged occasionally in bands and whorls. In patches at a deeper layer, closely packed small rounded

cells could be seen. These took the dye more faintly and proved to be the so-called pear-shaped cells.

The impression gained from this study was that through instrumentation and handling a considerable degree of derangement of cells had occurred and that it would be advisable to observe the action of dye applied directly to the exposed, living ureteral epithelium.

Action of Dye on Living Ureteral Epithelium: By means of operative technic B the ureter was observed in segments, the procedure being started with the lower end and repeated almost as far as the renal pelvis. The selected ureteral site was mobilized by incising the peritoneum on

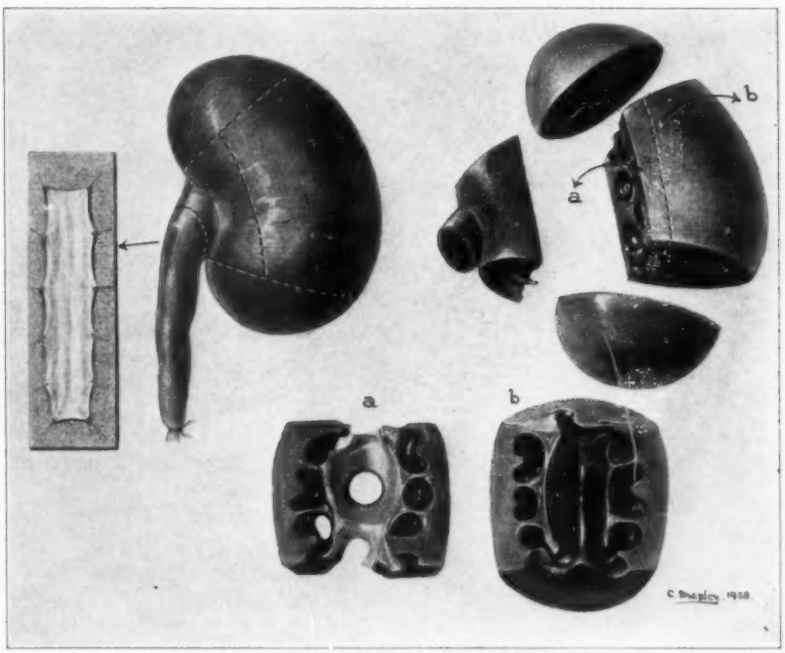

Fig. 4.—Procedure adopted in preparation of the fixed specimen for study. Freehand or frozen sections may be made subsequently as desired.

the outer side and displacing it medially. A small, thin piece of cork covered with white paper was slipped under the freed segment. The portion of ureter over the cork was incised longitudinally to a sufficient extent to enable a flat field of ureteral lining to be exposed by gentle retraction. In fixing the margins to the underlying cork by fine pins, care was taken to avoid any tension that would impair circulation. Under direct binocular control a very small drop of dye was placed gently on the epithelial surface and was watched. The changes observed were as follows:

As the dye began to spread, it appeared to pass into a network of fine channels with clear interspaces. The spaces were fairly uniform in size but varied in shape, the majority being pentagonal or hexagonal. After a few minutes this fine, apparently intercellular network tended to be obscured by a subjacent spread of diffuse dye into well defined areas with angulated margins. After a few more minutes points of intenser staining appeared throughout this area, and presently there was revealed a pavement type of epithelium with clear spaces between the

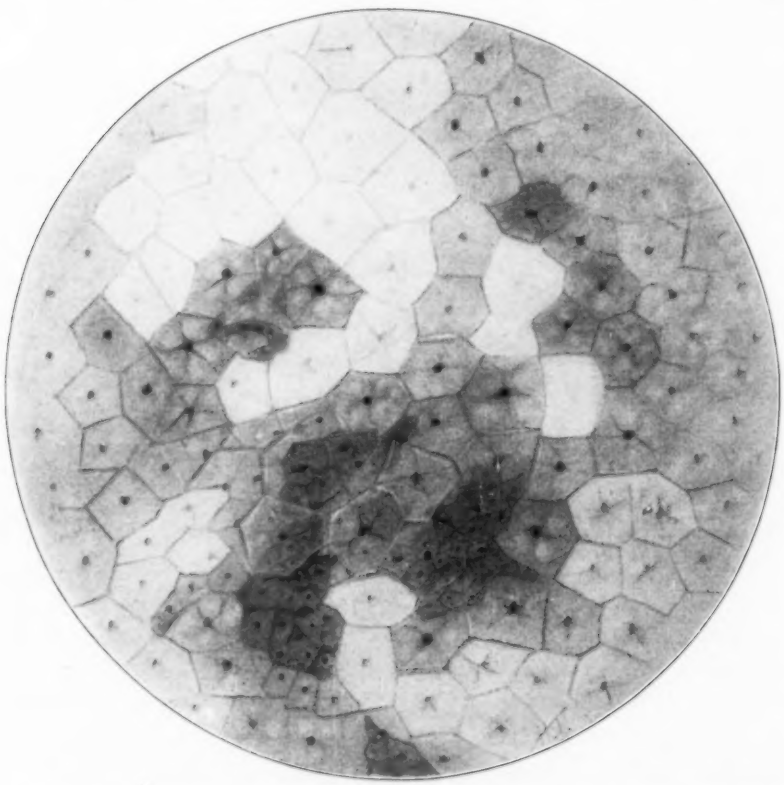

Fig. 5.—Ureteral epithelium in total obstruction. This is a composite drawing of the altered cellular arrangement as viewed from the surface. The oldest and most superficial transitional cells, not having absorbed dye or having absorbed it only faintly, show up clear with pale nuclei. They tend to preclude dye from penetrating to underlying cells. From areas where these cells have desquamated, varying intensity of absorption occurs. The youngest generation of small, flat cells takes a relatively deep stain. A number of the large cells have a stellate appearance, caused by the presence of subjacent small rounded cells.

cells and well stained large nuclei, some of which were double. Variation in the size of these cells was noted, in that as diffusion of the dye continued relatively smaller ones became evident. Subsequently, scattered

areas of densely packed, small rounded cells could be seen. These absorbed the dye rather faintly and were about a third the size of the epithelial cells previously described.

To determine the relation of these cell types a small pledget of cotton wool moistened in saline solution was gently applied to the well defined original network. Instantly there occurred a desquamation of clear cells, obviously a keratinous layer. After the removal of this layer, the staining of the subjacent layer was more rapid, the intercellular spaces soon showing as a clear, roughly hexagonal-meshed network against the deeply stained cells of the transitional epithelium. When drops of physiologic solution of sodium chloride were gently applied to this layer of cells, it was noted that individual cells easily became detached and floated away. When one continued to remove these cells and apply fresh dye, the small rounded cells became evident. This layer was more firmly fixed and could not be detached with anything like the ease with which the first two layers were detached.

(*b*) *Renal Absorption.*—In animals with total obstruction of the left ureter for periods varying from a few minutes to a month or more, the left kidney and ureter were exposed as described for operative technic B. Ether was first given, and narcosis was maintained as required by injections of pentobarbital sodium. Some of the observations were continued at intervals for a total period of twelve hours.

Immediately after introduction of the dye into and religation of the ureter, observation was centered on two sites: (*a*) the lymph channels of the renal pedicle and (*b*) the surface of the kidney.

(*a*) By removing the peritoneal covering and gently separating the components of the renal pedicle one can identify the lymph channels. The lymph vessel, with its translucent walls through which the fine bicuspid valves can readily be seen, is a characteristic structure. At the pedicle the lymph channels vary in number and manner of distribution but are as a rule associated with the renal artery and lie between it and the vein.

As a precautionary measure, simultaneous dual observation was made with one binocular microscope trained on the lymph vessels of the pedicle and another focused on the surface of the kidney. It was hoped that in this way any rapid temporary transit of dye through the lymph channels would be detected.

(*b*) In the presence of hydronephrosis the lymph channels coursing over the surface of the kidney in the false capsule appear to be somewhat more distended and easier of identification than in the normal kidney. During the initial period after the introduction of dye these capsular lymph channels were watched for any evidence of conveyance of the dye, and the renal cortex was coincidentally observed for tubular

absorption. As tubular absorption is patchy in distribution it was necessary to be constantly reviewing a large surface of cortex, particularly the middle third zone, in which the absorption occurs more frequently. The first evidence was mottled pallor around certain groups of renal lobules. Looking down on the surface, one could usually discern the terminal end of a main collecting duct in the center of one of these paler lobules. It showed as a small rounded dot. It became more pronounced because of ascending dye in its lumen, and presently its terminal subdivision into two or more irregularly arched connecting and distal convoluted tubules was made visible by the contained dye. An area showing a group of absorbing tubules presented the appearance below the true renal capsule of an irregular cluster of uneven, inverted U-shaped bends (fig. 6*a*). Owing to a number of easily appreciated factors, i. e., the degree of diuresis, the amount of dye introduced in relation to the total pelvic content, the degree of reduction of pelvic content after interference and the period of total obstruction, the time of appearance of dye in the tubules varied. In 2 instances it appeared within ten minutes. In the average obstruction of from five to seven days dye manifests itself in about thirty minutes. With hydronephrosis of about four weeks' standing the time of appearance is lengthened to approximately one or two hours.

The dye at first seemed to stain the tubule diffusely, but later an intensification of stain appeared at the basement membrane, and individual basal cells could be noted (fig. 6*b*). At this stage, small well stained objects, such as granules or portions of cells, were frequently to be seen within the tubules. At the outset of this study no particular attention was paid to these except to note that they were probably basal cells so situated on the wall of the tubules as to present a surface view. More consistent observation, however, revealed that some of these particles were not stationary as had been assumed. In a number of instances such particles were observed to ascend into the loop of the tubule, traverse its visible extent and after a short pause return to the starting point. This excursion was repeated at brief intervals. The rhythm of these movements was noted and was observed to coincide with the ureteral peristaltic waves, which occurred every thirty to thirty-five seconds. The impression gained was that in the presence of hydronephrosis the main collecting ducts and their immediate subdivisions, together with the connecting and distal portions of the tubule units, are dilated and are in fluid continuity with the pelvis and ureter. Thus, alterations in the content pressure of the latter are transmitted directly to the periphery of the renal cortex.

Although it was hoped that it might be possible to observe by transference of dye the mechanism of absorption from the tubule back into

the general circulation, no definite data could be obtained. It was noted, however, that after thirty minutes or so the tissues in the vicinity of tubules which had taken up dye began to show a pale tinge of the dye. This pale coloring appeared to be in the intertubular spaces, but whether in lymphatic or venous radicles it was impossible to say (fig. 6*c*). At the time of its appearance and subsequently, the lymph channels of the renal pedicle were carefully watched for a possible trace of color in their contents, but without any convincing result.

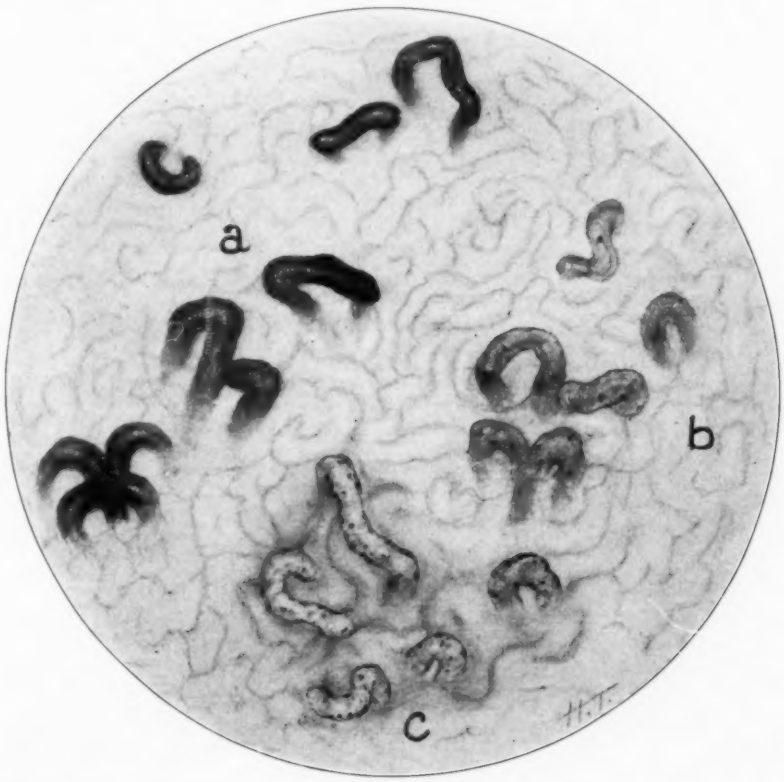

Fig. 6.—Tubular absorption as seen on the surface of the renal cortex. This is a composite drawing of three small groups of tubules at varying stages of absorption of dye. The point marked *a* denotes absorption during the initial period. The tubules show marked content of dye. The point marked *b* denotes absorption during the intermediate stage. The content of dye is less apparent; the tubular walls and the cells are becoming stained. The point marked *c* denotes absorption in the late stage. The lumen of the tubule is almost free of dye, while discrete cells and the walls of the tubule are deeply stained.

As has been indicated, the spleen and a portion of the liver were removed in each instance when the animal was killed. When dyes had been employed, careful study of sections of these organs failed to show any evidence of dye.

LINING EPITHELIUM OF THE UPPER PORTION OF THE URETER AND THE RENAL PELVIS AFTER VITAL STAINING

Dissections of the rabbit kidney after vital staining and fixation revealed certain interesting features with regard to the lining epithelium of (*a*) the pelvic portion of the ureter, (*b*) the pelvis and (*c*) the papilla.

(*a*) *Pelvic Portion of the Ureter.*—The pelvic portion of the ureter (fig. 7), or that portion which expands within the renal hilus to

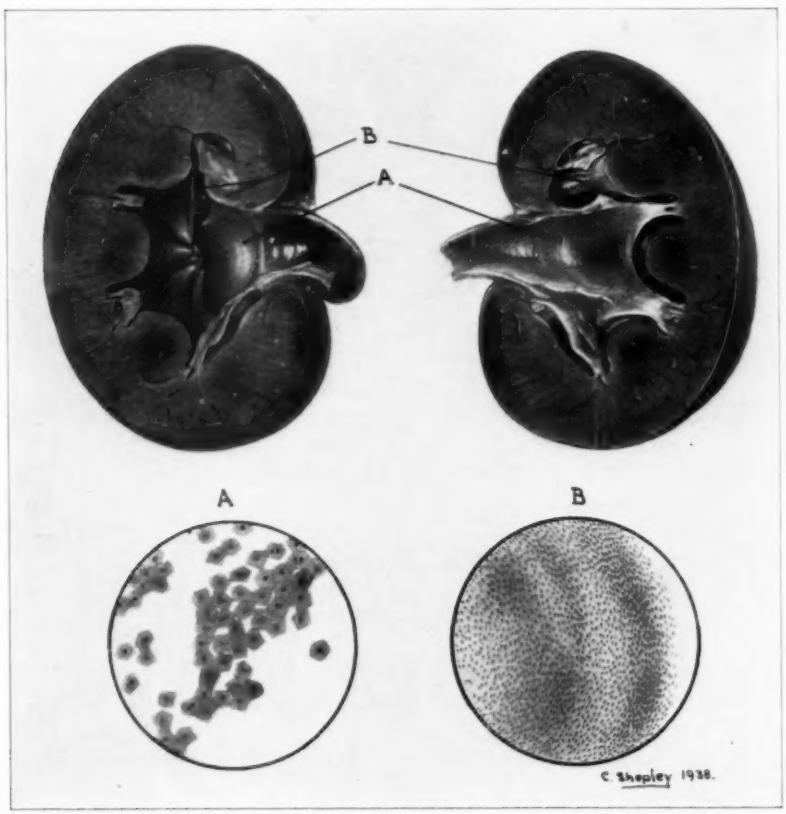

Fig. 7.—Early stage of hydronephrosis (rabbit). The longitudinal section discloses the components of the renal pelvis. *A*, pelvic zone of the ureter. *B*, parenchymal walls. In the circles the types of epithelium characteristic of these areas are correspondingly indicated.

accommodate the papilla and terminates in a fluted manner around the sulcus at the base of the medullary pyramid, has a lining epithelium similar to that of the rest of the ureter. It is capable (probably to a lesser extent than is the ureter proper) of expansion and contraction; consequently, the lining epithelium must be able to meet for a time the extra stress incurred by total obstruction.

After obstruction had been present for about a week or more, the transitional epithelium of the lining was observed to present definite changes. The previously uniform layer of cells showed scattered distribution. The vital staining was taken up by cells individually or in groups, intervening spaces being left completely clear, with no evidence of absorption of dye. The remaining cells usually showed either larger single nuclei than normal or double nuclei (fig. 8*A*). The stellate appearance not infrequently noted in the normal state was at times pronounced. This suggests that dye had probably passed from the overlying flat cell into the interspaces between the pear-shaped cells underneath. In some specimens taken after long obstruction most of the typical large superficial cells had disappeared, and in their place were

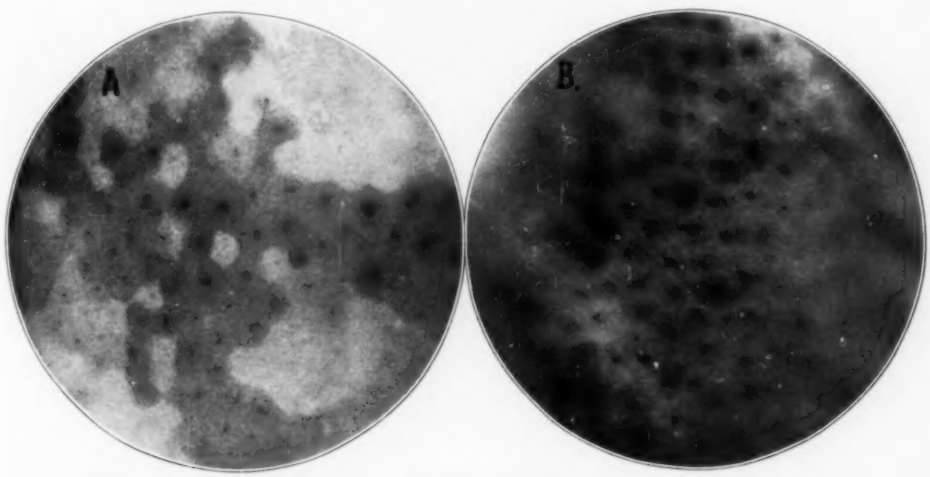

Fig. 8.—Photomicrograph of lining transitional epithelium in a case of total obstruction (surface view). *A*, pelvic zone of the ureter. *B*, ureter.

smaller cells of various shapes (figs. 9*A* and 9*B*). These frequently grouped themselves into peculiar whorl formations, spirals or bands (fig. 10).

(*b*) *Pelvis.*—The lining of the pelvic walls (fig. 7*B*) and the partition-like extensions which unite with the ureteral expansion and enfold the main subdivisions of the renal artery and vein on either side showed a uniform epithelial covering in which an occasional small pear-shaped cell became outlined with dye. This actively absorbing cell was slightly columnar and after becoming stained protruded somewhat from the general surface. It differed from any of the transitional cell types and was much smaller. After vital staining the number outlined was relatively small in the lower aspects of the calices, but such cells appeared to be invariably more numerous in the upper zones and particularly at

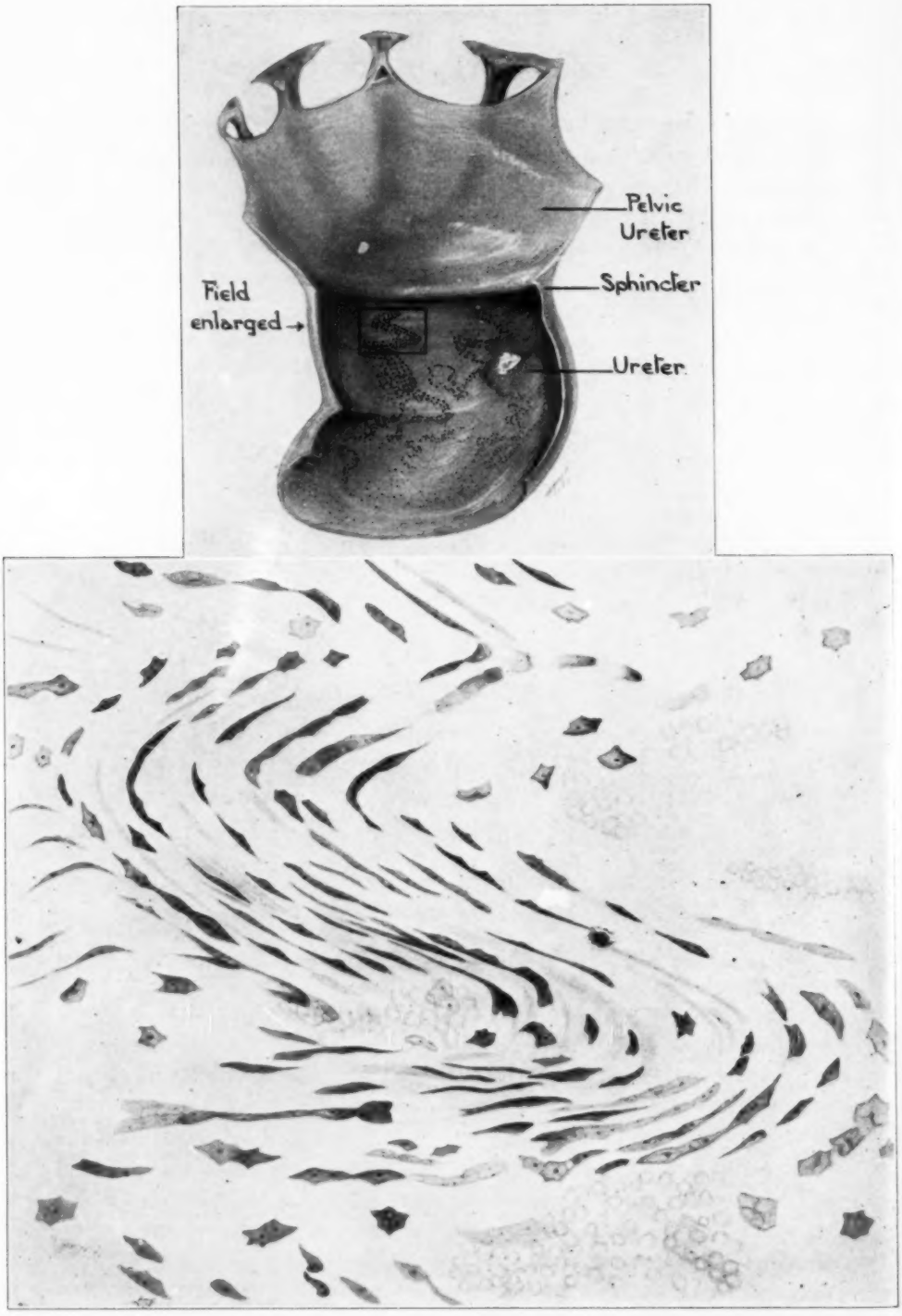

Fig. 9.—*A*, chart to act as a guide to figure 9 *B*. *B*, transitional epithelium at the pelvoureteral zone. Note the derangement consequent on total obstruction. Considerable desquamation has occurred, exposing areas of the faintly staining, small rounded cells of the basic layer. The distortion of the cells is probably due to the abnormal pull exerted by the fibrils which under normal conditions maintain the relation of this type of epithelium despite a considerable range of expansion and contraction.

the angle of reflection, where the lateral walls meet the base of the papilla. In many instances the extent of absorption of dye by the cells in these special sites was intense and usually was associated with infiltration of dye into the subjacent tissues. Despite careful search, no definite evidence has so far been obtained of any lymphatic association, but the picture suggests such a probability.

(*c*) *Papilla.*—From observations made on a series of renal papillae after varying periods of total ureteral obstruction it is evident that this structure is almost the pivotal point in the distending renal pelvis. It is subject to a progressive outward radial pull, and the consequent tension is liable on any extra stress to cause splitting of the overlying mucosa and even rupture of the papilla (figs. 11 and 12). With vital staining

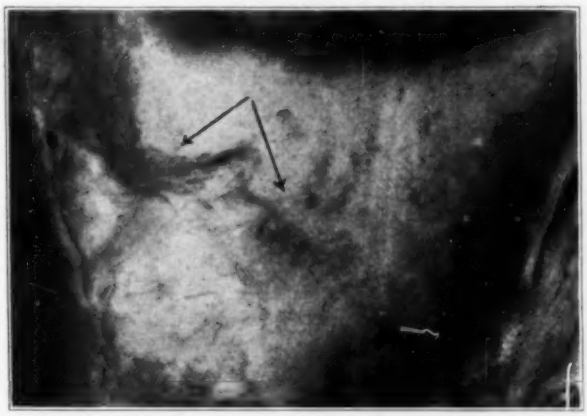

Fig. 10.—Pelvic portion of the ureter. The illustration shows a portion of the wall, surface view. Vital staining was used. The transitional epithelium shows considerable derangement, with a limited group of stained cells forming a wavy band, as indicated.

the epithelium covering the papilla presents points of interest which are not apparent in ordinary paraffin sections. After the specimens were fixed in Jores solution, frozen or freehand sections were made and examined under varying powers of the binocular microscope. By this means it was felt that distortion was minimized and a three-dimensional impression gained of the grouping and character of the cells. The manner of absorption of dye shown by the cells of this particular region tended to strengthen the impression of a definite selective action. Only a certain number of the cells absorbed dye, and those doing so were fully stained, whereas adjacent, apparently similar cells remained clear. The contrast, accordingly, offered greater facilities for observing the type and distribution of the cells.

It was noted that the stained cells covering the papilla were somewhat wedge shaped, with nuclei toward the broad end. They were arranged in a definite columnar fashion, particularly at the summit, around the openings of the main collecting ducts (fig. 13). From the summit the length of the cells gradually lessened, and as the papillary

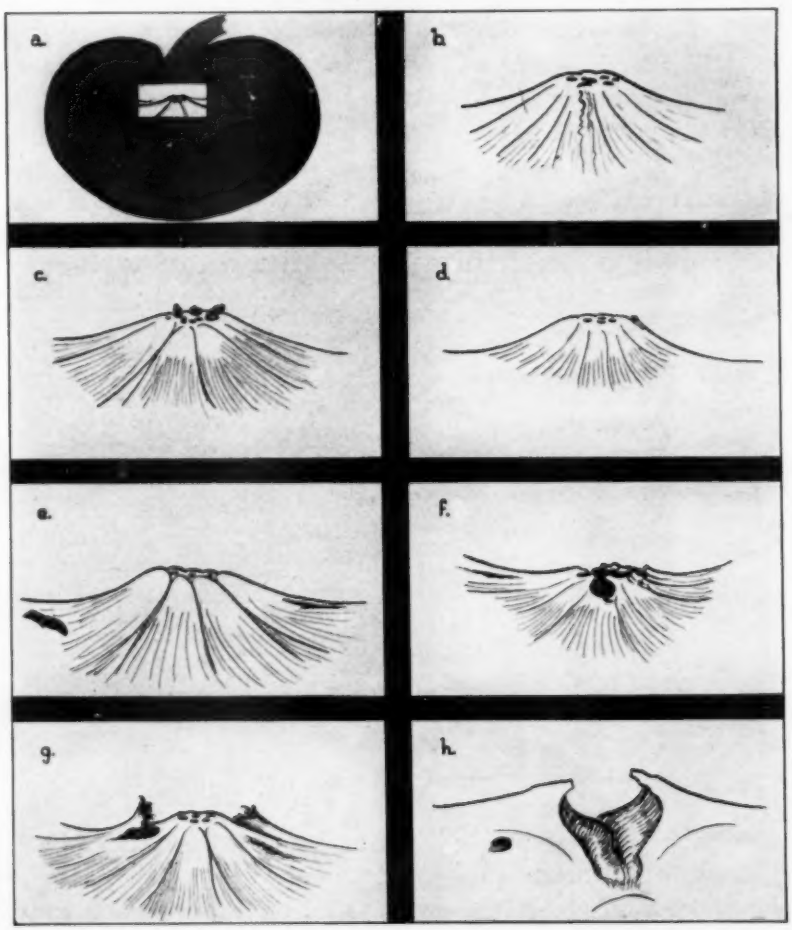

Fig. 11.—Renal papilla in a case of hydronephrosis. Drawing *a* denotes the area depicted; *b*, the tip of the papilla, showing the mouths of the main collecting ducts; *c*, cellular débris and dye plugging the mouths of three main collecting ducts; *d*, papilla presenting a minute epithelial tear on the right side; *e*, two areas of trauma on either side toward the papillary base; *f*, trauma involving the mouths of the duct; *g*, tears with retraction on the lateral aspects; *h*, gross splitting of the papilla.

base was reached the usual small, almost pear-shaped cell constituted the epithelium, in continuity with that of the rest of the pelvic cavity (fig. 15).

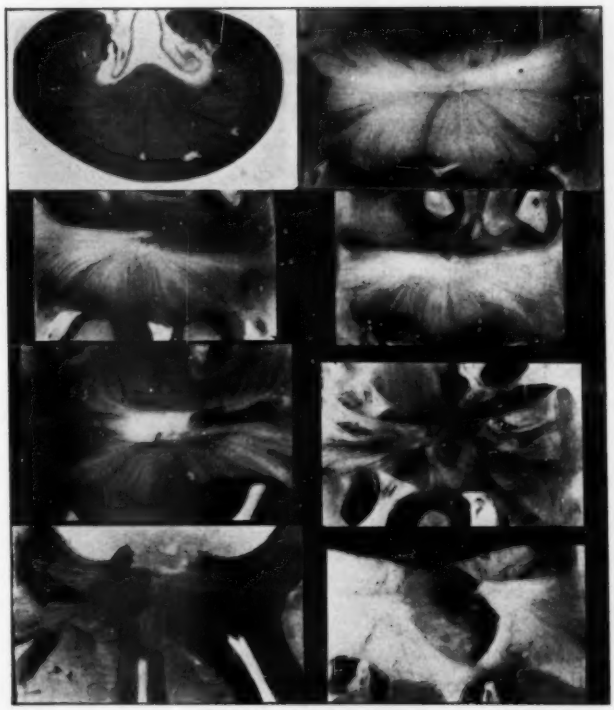

Fig. 12.—Renal papilla in a case of hydronephrosis. The same specimens similarly arranged, which are diagrammatically shown in figure 11.

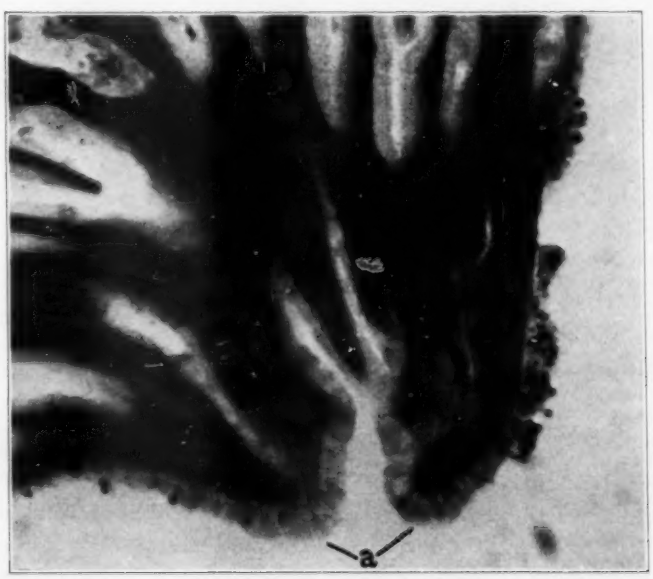

Fig. 13.—Photomicrograph of the tip of the renal papilla (frozen section). Dilatation of the mouths of a main collecting duct, consequent on hydronephrosis, is evident, and the columnar cells (*a*) which have absorbed dye present radial striation.

Longitudinal sections of the papilla revealed that these peg-shaped cells were present in the walls of the main collecting ducts and were interspersed with cells of the cuboidal type (fig. 14 *A*). As the cuboidal cells remained clear, the deeply stained peg-shaped cells showed up in marked contrast. They extended from the lumen of the duct and narrowed down as they reached the basement membrane. Many of them showed a definite narrow band of deeper staining at the wider, free end, which abutted on the lumen of the duct. The nuclei were mainly central or toward the lumen. In some respects these cells resembled the columnar cells of the intestine. The number of such readily stained cells became less as the base of the pyramid was reached. Their presence in the otherwise clear collecting ducts gave a ladder-like appearance

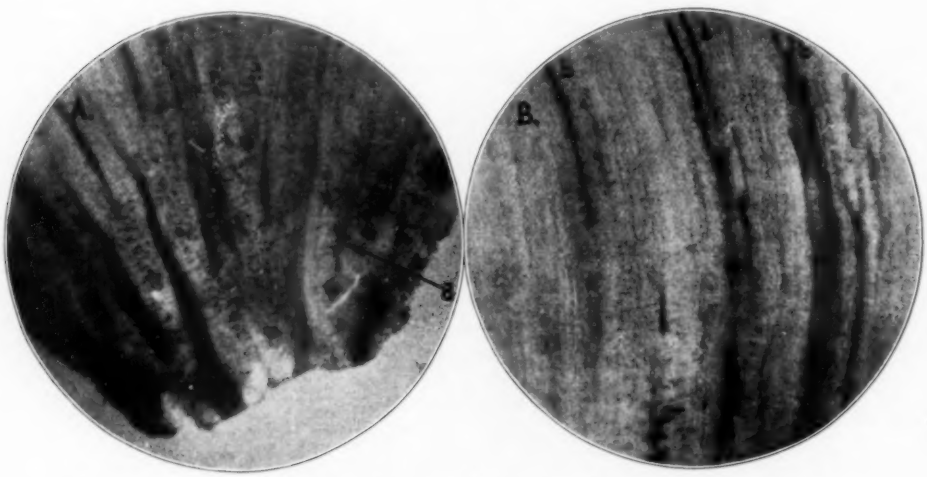

Fig. 14.—Collecting duct system (photomicrographs of frozen sections). *A*, columnar cells (*a*) which have absorbed dye, interspersed with clear cuboidal cells lining the main collecting ducts at the renal papilla. *B*, the collecting duct system toward the base of the papilla. The finer subdivisions of the collecting ducts in this region show absorption of dye by cells of a smaller, more rounded type (*b*).

in longitudinal section (fig. 15 *g*). In ordinary stained paraffin section the cells were somewhat pear shaped, with nuclei usually definitely nearer the lumen of the duct than the basally situated nuclei of the cuboidal cells. It was noted that in the areas where these columnar or peg-shaped cells had taken up a marked degree of staining the immediate underlying tissue also showed appreciable absorption of dye. The underlying tissues of the papilla showed deep staining in instances in which tears had occurred in the overlying epithelial layer or in which there had been direct splitting of the papilla itself.

From near the base of the medulla the subdivisions of the collecting ducts showed a transition from the columnar form of cell to a small rounded type which is characteristic of the ducts from this level outward to their ultimate subdivisions in the cortex (fig. 14 *B*).

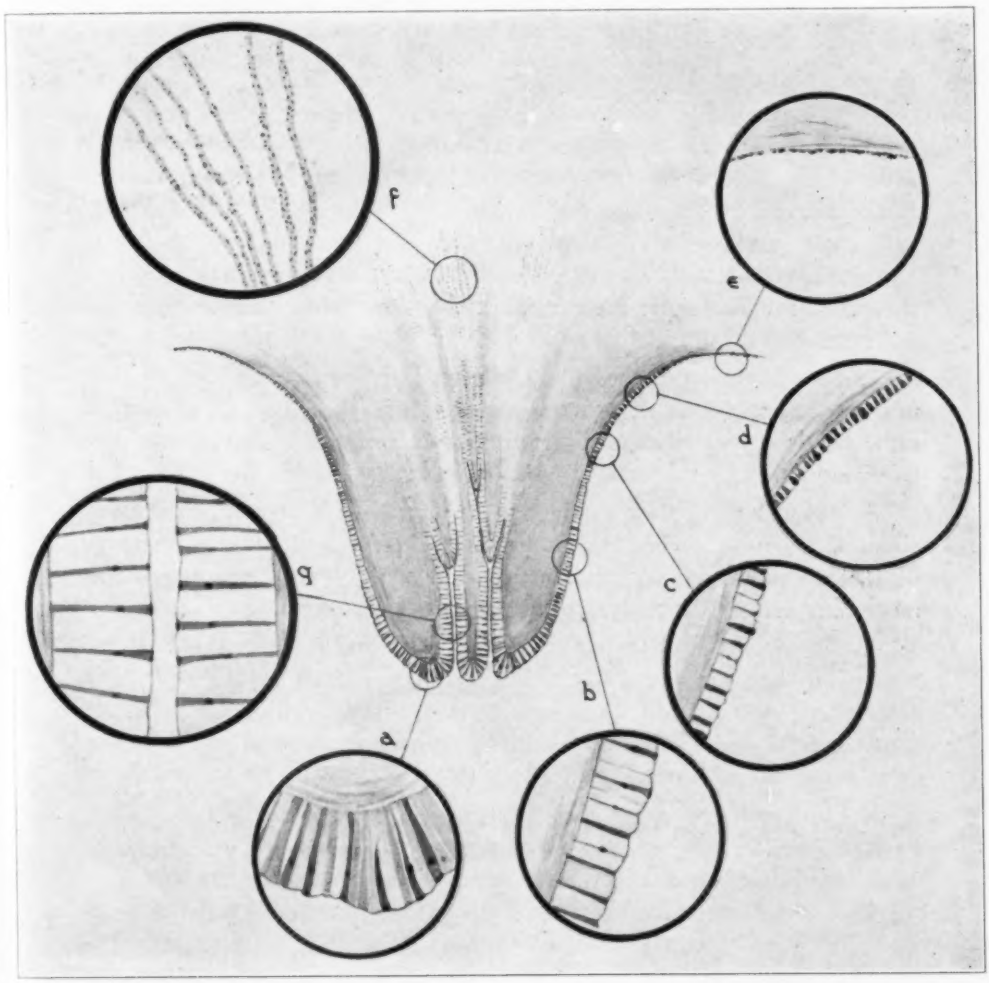

Fig. 15.—Semidiagrammatic representation of the renal papilla (rabbit) in longitudinal section. The covering epithelium of the papilla and the lining of the duct are shown after vital staining. The types of individual cells which absorb dye are depicted by a series of enlarged fields from sites indicated as follows: *a*, tip of the papilla; *b*, *c* and *d*, graded epithelium of the lateral walls; *e*, angle of reflection (these cells will be seen to be similar to those of the pelvic lining); *g*, main collecting duct; *f*, lesser collecting ducts at the papillary base.

Although during life the lymphatics of the renal pedicle were kept under constant observation, no obvious evidence of transmission of dye was noted in these experiments. It may be that lymphatic drainage from these areas is relatively slow. The possibility has been cited of an intrarenal lymphatic system which drains directly into the renal veins, as distinct from an extrarenal or superficial system which drains into the large vessels accompanying the renal pedicle. Confirmation of this is needed.

CONCLUSIONS

1. There is rapid absorption from a totally obstructed hydronephrotic sac into the general circulation of such agents as uroselectan B (known in the United States as neo-iopax) and phenolsulfonphthalein. Indigo carmine is similarly eliminated, but more slowly. Interruption of the lymphatic vessels at the renal pedicle produces no appreciable effect on the rate of absorption; an exclusively venous route, therefore, seems indicated.

2. Rapid lymphatic absorption follows intertubular injection of dyes into the superficial aspects of the cortex. Studies of the ureter and the renal pelvis suggested that absorption from the walls and lumen is relatively slow.

3. Tubular absorption of dyes from the pelvis is usually manifest in about thirty minutes but can occur more rapidly with total obstruction of four to five days. With longer periods of obstruction an hour or more may elapse before dye is evident at the cortex.

4. Suggestive evidence was obtained in several instances of obstruction of five to eight days' standing that the varying pelvic pressure occasioned by peristaltic movements is transmitted directly by fluid continuity from the pelvis to the distal convoluted tubules in the superficial zones of the cortex.

5. Studies of the lining epithelium of the ureter and the renal pelvis were made after vital staining, and the types and reactions of the cells were noted. A selective action with regard to immediate absorption is suggested. Certain cells distributed over the renal papilla as well as in the main collecting ducts are of a columnar type, resembling those of the gastrointestinal tract.

ABSTRACT OF DISCUSSION

DR. FRANK HINMAN (San Francisco): Knowing the skill and the meticulous care with which Dr. Morison works, I am sure there can be no question of the accuracy of his observations. When it comes to their interpretation, however, I think there is room for a difference of opinion.

Vital and intravital stains have been a bone of contention from the time they were first used, and whether staining by these methods means contact stain, phagocytosis, cellular secretion or cellular absorption is usually open to question.

So true is this that the most recent book on the physiology of the kidney (Smith, H. W.: The Physiology of the Kidney, London, Oxford University Press, 1937) dismissed the finding of vital stains in one paragraph, stating that the interpretations are so various and uncertain as to prove nothing with respect to the physiology of the kidney.

Now this has nothing particularly to do with the original work of Dr. Morison. He has shown excellent sections of the pelvis and of the collecting tubules, but I think that the question whether his demonstration establishes a route of absorption or the tidal flow in hydronephrosis is open to discussion.

Let me review briefly some of the points against cellular reabsorption as a factor of moment in the explanation of the phenomenon of hydronephrosis.

Hydronephrosis with complete ureteral obstruction is unique. Complete obstruction of the ducts of other glands brings about primary atrophy, whereas only exceptionally, in a few experimental animals does primary atrophy follow complete obstruction of the ureter.

The active portions of the renal tubule are the glomerulus, the proximal convolution, the loop of Henle and the distal convolution. The remaining parts of the system are purely conductive and have no more to do with the formation and secretion of urine than does the renal pelvis, the ureter or the bladder.

When the ureter is obstructed there is at once a back pressure on the secreting and conducting parts of the tubule, and this increases until it equals secretory pressure; nevertheless, the formation of urine continues, with dilatation and progressive atrophy of the secreting portions of the tubules, until at the end of the process only the glomerulus and a straight tube remain.

A section of a hydronephrotic sac after intravital staining shows that the convoluted tubular area takes up the stain, thus presumably demonstrating vital activity of the cells lining the tubules. This activity is thought to be secretory. Absorption occurs mostly in the loop of Henle and in the distal convolution. Physiologists now speak of the clearance of substances; for example, the clearance of uric acid, of chloride, of creatinine and of other substances. The concentration of any such substance in the urine multiplied by the amount of urine formed in the unit of time, divided by its concentration in the blood, measures its clearance during this period. To what extent the clearance of any particular substance is affected by filtration, secretion and absorption has not been fully determined, though the fact that these three processes occur has been fully established.

The final stage of hydronephrosis, with complete obstruction of the ureter after the process of group destruction and group preservation, has been demonstrated by Dr. C. M. Johnson. The tubules were dissected out under the microscope after maceration from an arterial injection of hydrochloric acid. All of the active secretory portions of the tubular system had disappeared, and only the glomerulus, with a relatively short conducting tube, was left; yet the glomerulus still filtered a certain amount of urine, keeping up the pressure in the sac, which continued to enlarge slowly until even the glomerulus had become atrophied. This marks the stage of complete hydronephrotic atrophy.

An experiment carried out in conjunction with Dr. Carroll has its significance in reference to the role of absorption in hydronephrosis. Ligatures were so placed as to obstruct the collecting ducts of the papilla in the kidney of the rabbit without obstructing the ureter and so placed also that the circulation of the kidney was in no way hampered. Only the collecting ducts, which carry the urine from the secreting portion to the pelvis of the kidney, were obstructed. A series of sections made seven, forty-two, eighty-four and one hundred and eighty days thereafter showed the results, and each was compared with a hydronephrotic specimen

taken after a similar period of ureteral obstruction. Atrophy of the substance of the kidney following obstruction of the duct resembles primary atrophy more than hydronephrotic atrophy. In the experiment referred to, at eighty days almost all secreting elements had completely disappeared. Atrophy is much more rapid than after ureteral obstruction.

As a final argument against cellular activity as a route of reabsorption, it is known that in the presence of hydronephrosis there must be not a selective but a gross back flow or absorption from the renal pelvis, if for no other reason than that the content of the sac at any stage of hydronephrosis is similar in composition to that which the kidney would secrete at the time if the obstruction were removed, provided the kidney were still capable of secretion.

It is also known from studies on back flow (whether pyelovenous, pyelolymphatic, pyelotubular, tubulovenous, tubulolymphatic or interstitial) that the pressure required to produce this back flow diminishes as the period of ureteral obstruction lengthens. It is known, too, that intrapelvic pressure falls with the duration of hydronephrosis. These two facts seem to agree.

Lymphatic back flow explains satisfactorily the condition of chyluria. The chyle which cannot find normal exit by the thoracic duct flows back into the pelvis of the kidney, and this lymphatic communication with the pelvis can often be demonstrated pyelographically. If chyle can flow back from lymphatics into the pelvis after obstruction of the lymphatics, it seems reasonable to suppose that the urine in the pelvis can flow into these lymphatics after obstruction of the ureter.

Cellular activity of the tubules would seem to perform only a minor and unessential part in the pathogenesis of hydronephrosis.

The pictures Dr. Morison has shown provide an excellent demonstration of the collecting system.

DR. CHARLES P. MATHÉ (San Francisco): It has been a great pleasure to hear Dr. Morison describe his splendid experimental study on the routes of absorption of dyes in the presence of hydronephrosis with total obstruction of the ureter. Experiments on various phenomena occurring in association with hydronephrosis were initiated some years ago, when Dr. Morison was a member of the urologic staff of the University of California Medical School. As a former staff confrère, I wish to felicitate him on the splendid work that he has continued and has since accomplished in this field.

His findings are significant. In experimenting with the dyes commonly used for studying renal function he observed that uroselectan B and phenolsulfonphthalein are rapidly absorbed by the general circulation when injected into a totally obstructed hydronephrotic sac, whereas indigo carmine similarly injected is eliminated much more slowly. Why should there be such a variance in the rate of absorption of phenolsulfonphthalein and of indigo carmine? In functional studies of the normal kidney, indigo carmine is usually observed to appear in three to five minutes after intravenous injection. The fact that interruption of lymphatic drainage had no influence on the rate of absorption shows that the lymphatics play a minor role in the absorption of dyes. Dr. Morison's observations on tubular absorption are interesting.

His experiments have cleared up the controversial subject of pyelovenous back flow. He has proved that such back flow is not normal but occurs only when trauma caused by overdistention of the pelvis forces injected material into the general circulation.

The clinical significance of the facts obtained by this series of experiments is important. In the presence of a closed, infected hydronephrotic lesion of the kidney, absorption of toxins resulting from bacterial invasion probably occurs in

the same manner as does absorption of dye. This explains the tremendous relief obtained by preliminary nephrostomy in the two stage surgical removal of a kidney involved in a closed pyohydronephrotic lesion.

Dr. Morison's experiments also point out the value of measuring pelvic capacity in order to determine the amount of an opaque medium that should be injected for the purpose of making retrograde pyelographic studies and the quantity of an antiseptic solution which should be utilized in carrying out pelvic lavage, because overdistention has been definitely shown to produce injury.

Dr. Morison's experimental work will prove to be of great clinical significance.

Dr. Duncan M. Morison (Edinburgh, Scotland): For those who are not particularly interested in experimental work and prefer clinical data, a histophysiologic presentation tends to be tedious.

My paper was put forward purely as an interim report on the work which my associates and I are pursuing. We hope in time, by using such mediums as dyes, to trace the routes by which infection is probably carried from the walls and lumen of the upper portion of the urinary tract to the general system. Much yet remains to be done, and I should be grateful if at any time when any one has ideas on the subject he would communicate with me.

EFFECT OF EXPERIMENTALLY FORMED TUMORS ON THE MUSCULOSKELETAL SYSTEM OF THE RAT

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AND

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NEW YORK

There are many published studies of the development of malignant tumor after the topical application or injection of anthracene derivatives.[1] Only a few of these investigations, however, have dealt with attempts to produce such a tumor in or near a bone or a joint.[2] The present study is devoted to this point and specifically to the effects of such a tumor on skeletal tissue, as noted roentgenographically and histologically. In the course of the experiments several noteworthy complications appeared in addition to the tumors. Routine histologic examination of the latter with the aid of hematoxylin and eosin staining was supplemented by comparative studies made with the Laidlaw silver method [3] and with the so-called fluorescent technic.[4]

METHOD

The activating agent used was 1,2,5,6-dibenzanthracene. Three milligrams of dibenzanthracene was dissolved in 1 cc. of benzene or suspended in 1 cc. of melted lard.[5] Injections were made into 35 adult albino rats each weighing about 150 Gm.[6]

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From the Laboratory Division, Hospital for Joint Diseases, New York.

Aided by a grant from the Committee on Scientific Research of the American Medical Association.

1. Cook, J. W., and Kennaway, E. L.: Chemical Compounds as Carcinogenic Agents, Am. J. Cancer **33**:50 (May) 1938.

2. (*a*) Lacassagne, A.: Essais de production de cancer chez le lapin au moyen du 1:2:5:6 dibenzanthracène, Compt. rend. Soc. de biol. **114**:660, 1933. (*b*) Bernard, J.: L'érythro-leucémie expérimentale provoquée par le goudron, Sang **8**:28, 1934. (*c*) Ilfeld, F. W.: The Experimental Production of Visceral Tumors with Hydrocarbons, Am. J. Cancer **26**:743 (April) 1936. (*d*) Dunning, W. F.; Curtis, M. R., and Bullock, F. D.: Respective Roles of Heredity and Somatic Mutation in the Origin of Malignancy, ibid. **28**:681 (Dec.) 1936. (*e*) Brunschwig, A., and Bissel, A. D.: Production of Osteosarcoma in a Mouse by the Intra-Medullary Injection of 1:2 Benzpyrene, Arch. Surg. **36**:53 (Jan.) 1938.

(Footnotes continued on next page)

The accompanying table summarizes the procedure and the protocols for these 35 rats, in 16 of which tumor developed.

Macroscopic Findings.—The size of the new growths varied from that of a pea to that of an orange. Most of the tumors were firm and clearly delimited. On section they showed a gray fibrous tissue (fig. 1). A few scattered cysts and some yellowish necrotic areas were also encountered. In most of these, examination with filtered ultraviolet radiation revealed sites of golden fluorescence.

Roentgenographic Findings.—Roentgenographic examination of the rats revealed that most of the tumors, even though they abutted on skeletal tissue, had provoked little or no periostitis. Furthermore, none of the new growths themselves showed any bone formation.

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3. Stout, A. P.: Human Cancer, Philadelphia, Lea & Febiger, 1932.

4. Sutro, C. J.: Fluorescent Microscopy, Arch Path. **22**:109 (July) 1936.

5. (*a*) Cook, J. W.; Hieger, I.; Kennaway, E. L., and Mayneord, W. V.: Production of Cancer by Pure Hydrocarbons, Proc. Roy. Soc., London, s.B **111**: 455 (Oct. 1) 1932. (*b*) Andervont, H. B.: Production of Dibenzanthracene Tumors in Pure Strain Mice, Pub. Health Rep. **49**:620 (May 25) 1934.

6. Studies were also made on 19 additional rats, each of which was given 2 cc. of either warm lard or benzene, with or without dibenzanthracene. When dibenzanthracene was given, each cubic centimeter of menstruum contained 3 mg. of the drug. The injections were made into the right axilla, and the animals were killed at intervals ranging from four to two hundred and seventy days afterward. In these animals no tumors developed.

As long as two hundred and seventy days after the injection, filtered ultraviolet radiation sometimes still revealed the fluorescent dibenzanthracene in the cysts found at the site of injection ((*a*) Berenblum, I., and Kendal, L. P.: The Production of Tumors in the Fowl with a Colloidal Solution of 1:2:5:6-Dibenzanthracene, Brit. J. Exper. Path. **15**:366 (Dec.) 1934. (*b*) Lorenz, E., and Shear, M. J.: Studies in Carcinogenesis, Am. J. Cancer **26**:333 (Feb.) 1936. (*c*) Berenblum, I., and Kendal, L. P.: The Destruction of 1:2:5:6 Dibenzanthracene in the Mouse, Biochem. J. **30**:429 (March) 1936. (*d*) Sannie, C.: Carcinogenic Action and Absorption and Fluorescence Spectra of 1:2 Benzpyrene, ibid. **30**:704 (April) 1936. (*e*) Peacock, P. R.: Evidence Regarding the Mechanism of Elimination of 1:2-Benzpyrene, 1:2:5:6-Dibenzanthracene and Anthracene from the Blood Stream of Injected Animals, Brit. J. Exper. Path. **17**:164 (June) 1936. (*f*) Chalmers, J. G., and Peacock, P. R.: Further Evidence Regarding the Elimination of Certain Polycyclic Hydrocarbons from the Animal Body, Biochem. J. **30**:1242 (July) 1936. (*g*) Hieger, I.: On the Mechanism of Carcinogenesis by Chemical Compounds, Am. J. Cancer **28**:522 (Nov.) 1936; (*h*) The Fluorescence Spectrum of 3-4 Benzpyrene, ibid. **29**:705 (April) 1937). It was interesting to note that the granulation tissue examined twenty-five days after the first injection of benzene plus dibenzanthracene contained numerous mitotic cells, some of which were located in the lumens of capillaries.

Results of Injection of Dibenzanthracene in Rats

Group	Number of Rats in Experiment	Number of Rats with Tumor	Site of Injection	Total Number of Injections per Rat and Interval Between Injections	Contents of Each Injection	Duration of Experiment, Months	Site of Tumor	Size of Tumor	Microscopic Examination
A	4	0	Pericranial tissues in occipital region	6 injections (monthly)	3 injections each containing 1.5 mg. dibenzanthracene in 0.5 cc. of benzene; 3 injections each containing 1.5 mg. dibenzanthracene in 0.5 cc. of melted lard	8	No tumor		
B	3	2	Pericranial tissues in occipital region	6 injections (monthly)	3 injections each containing 1.5 mg. dibenzanthracene in 0.5 cc. of benzene; 3 injections each containing 1.5 mg. dibenzanthracene in 0.5 cc. of melted lard	7 and 15	Occiput	Pea and plum size	Cellular fibrosarcoma
C	4	0	Pericranial tissues in occipital region	4 injections (monthly)	2 injections each containing 1.5 mg. dibenzanthracene in 0.5 cc. of benzene; 2 injections each containing 1.5 mg. dibenzanthracene in 0.5 cc. of melted lard	8	No tumor		
D	4	3	Parosteal tissues of middle third of femur	5 injections (monthly)	3 injections each containing 1.5 mg. dibenzanthracene in 0.5 cc. of benzene; 2 injections each containing 1.5 mg. dibenzanthracene in 0.5 cc. of melted lard	8 and 10	Thigh, knee and leg	Plum size	Cellular fibrosarcoma
E	6	5	Lower lumbar vertebrae (spinous process)	6 injections (bimonthly)	1 injection of 1.5 mg. dibenzanthracene in 0.5 cc. of benzene; 4 injections each containing 1.5 mg. dibenzanthracene in 0.5 cc. of melted lard; 1 injection of 6 mg. of dibenzanthracene in 2 cc. of melted lard	12 to 14	Lumbar vertebrae region	Lemon size	Mixed cellular sarcoma
F	6	2	Region of knee joint	3 injections (bimonthly)	First injection, 1.5 mg. of dibenzanthracene in 0.5 cc. of benzene; second injection, 3 mg. of dibenzanthracene in 1 cc. of melted lard; third injection, 6 mg. of dibenzanthracene in 2 cc. of melted lard	15 and 19	Thigh, knee and leg	Plum size	Cellular fibrosarcoma
G	4	2	Major marrow cavity of tibia (surgical procedure)	One implantation	1.5 mg. dibenzanthracene in 0.5 cc. of lard	19 and 23	Thigh, leg and knee	Cherry and orange size	Cellular fibrosarcoma; in another, carcinoma in tibia secondary to primary intestinal carcinoma
H	4	2	Dorsal aspect of scapula	1 injection	6 mg. of dibenzanthracene in 2 cc. of lard	8 and 10	Axilla, ribs, lungs and humerus	Cherry to plum size	Cellular fibrosarcoma

Indeed, in some of the animals they were found to have eroded parts of the calvarium, the knee joints, the femurs, the tibias, the humeri, the laminas of the lumbar vertebrae and the ribs (fig. 2).

Microscopic Findings.—Histologic study revealed that most of the tumors were cellular fibrosarcomas. Some resembled rhabdomyosarcoma or myxosarcoma, and others somewhat resembled liposarcoma.

The cell nuclei of the new growths were of various shapes and types. Some were round, vesicular or flat. Others were multinuclear, and still

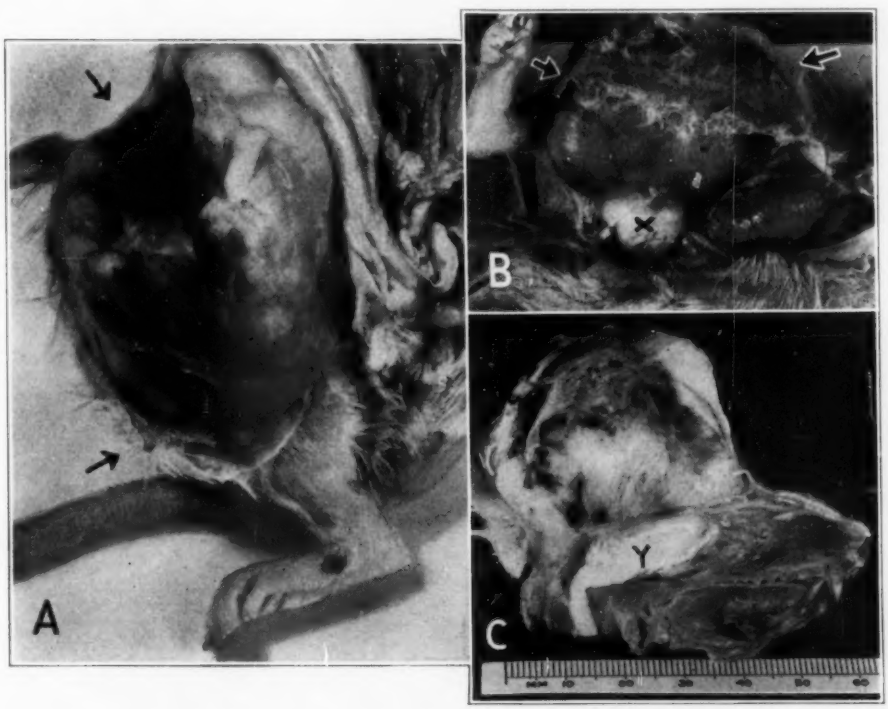

Fig. 1.—*A*, photograph of a rat (group D) with a sarcoma of the right thigh, knee and leg. The tumor has been bisected. *B*, photograph of another rat with a solid sarcoma about the right knee, leg and thigh. Note the cyst (*X*) in the right groin; it contained lardaceous material. *C*, photograph of the bisected head of a rat (group B) showing a fibrosarcoma on the calvarium. *Y* indicates the brain. Note the areas of hemorrhage in the tumor.

others resembled in certain respects the nuclei of bone marrow cells. Apparently the invading tumors had incorporated and activated the contiguous soft tissues and had thus induced the formation of sarcomas of the mixed cell type. In no case, however, was there any evidence of an osteogenic tumor (fig. 3).

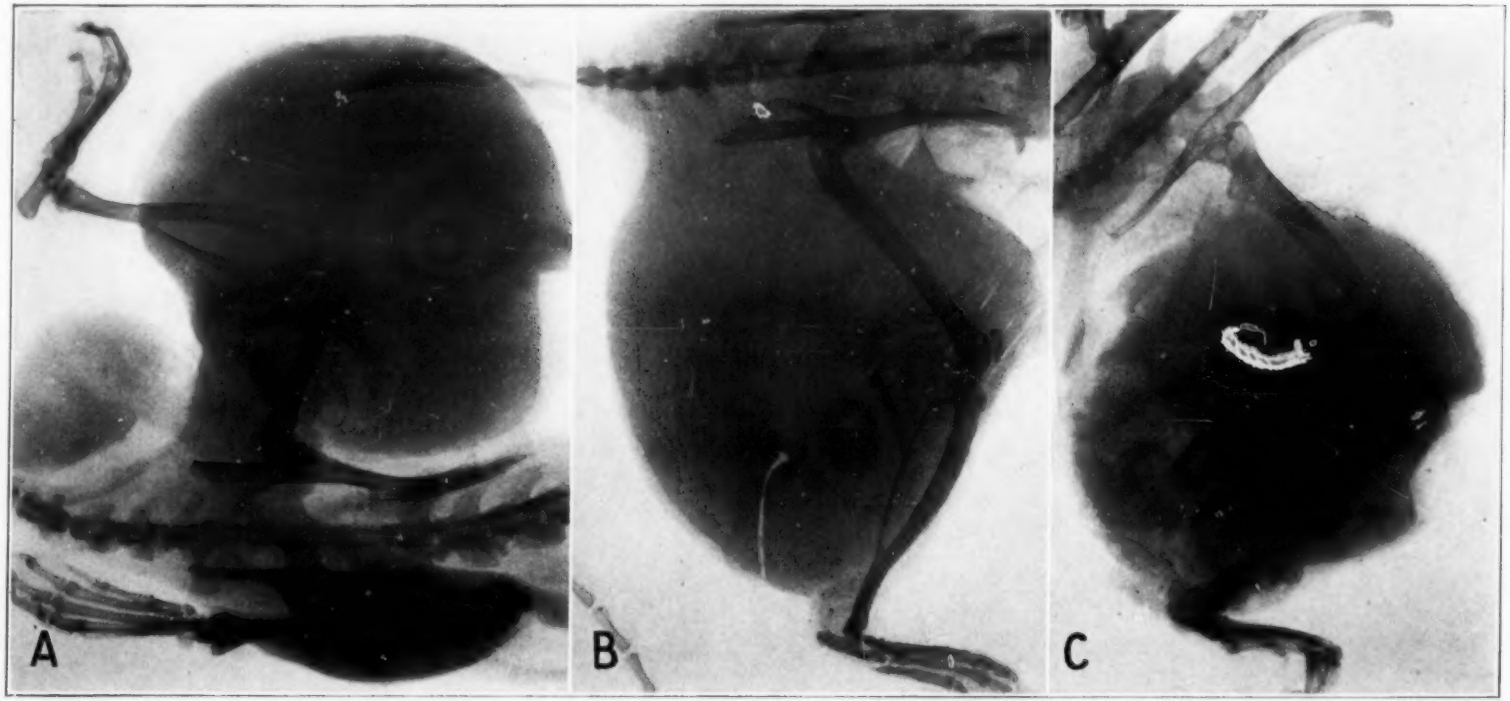

Fig. 2.—*A*, roentgenogram showing a tumor of the thigh, invading the right knee joint. Note the widening of the interosseous space and thickening of the fibula (Group D). *B*, roentgenogram showing a large tumor encasing the thigh and leg. Note the absence of periostitis (Group F). *C*, roentgenogram showing a large tumor invading the tibia, knee and femur. Dibenzanthracene was introduced into the marrow cavity of the tibia (Group G).

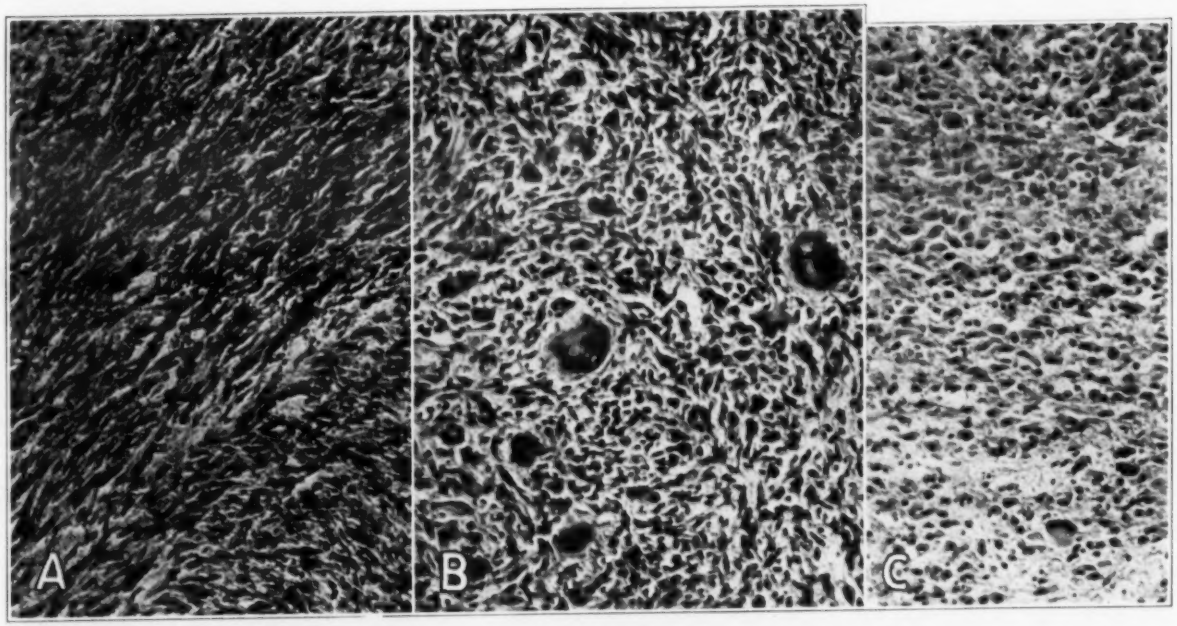

Fig. 3.—*A*, photomicrograph showing an area of fibrosarcoma. *B*, photomicrograph showing the large giant cells of a tumor. *C*, photomicrograph showing an area of immature tumor cells.

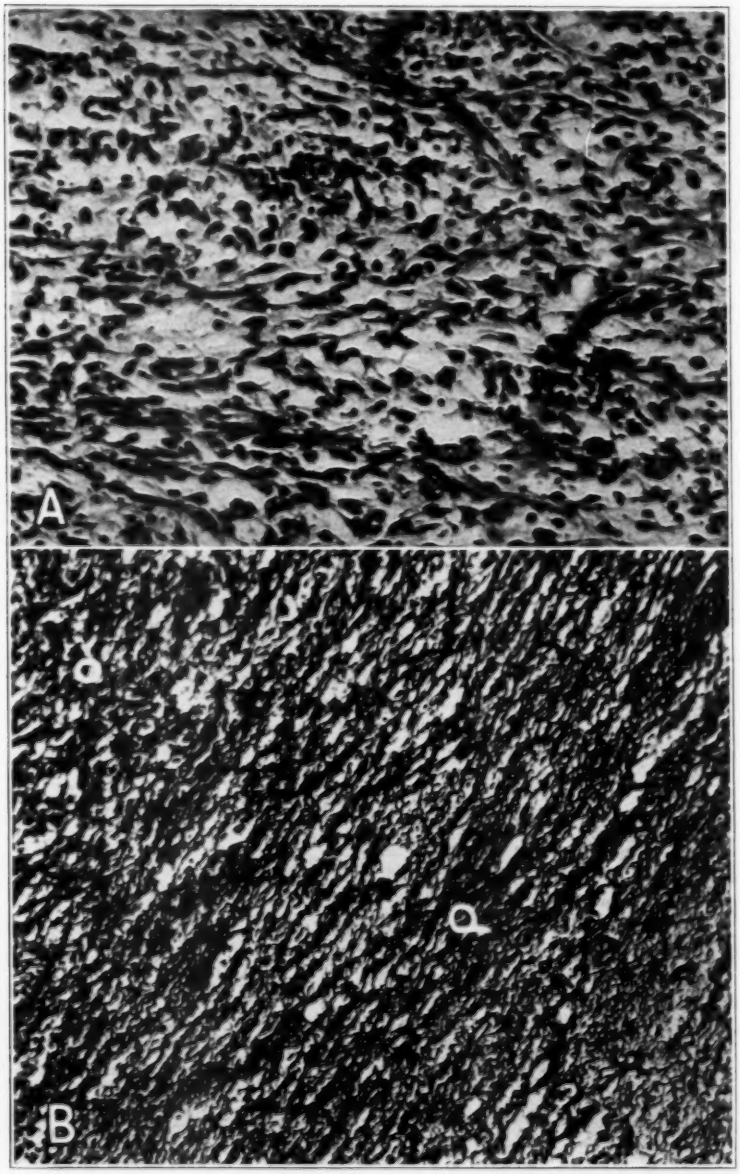

Fig. 4.—*A*, photomicrograph demonstrating an area of myxoma-like cells in the sarcoma. *B*, photomicrograph showing the Laidlaw silver reaction in the tumor. Note in the area marked *O* that the cells are positive and the fibrils are relatively sparse. In the area marked *a* the fibrils are closely set and numerous, but the nuclei do not stain.

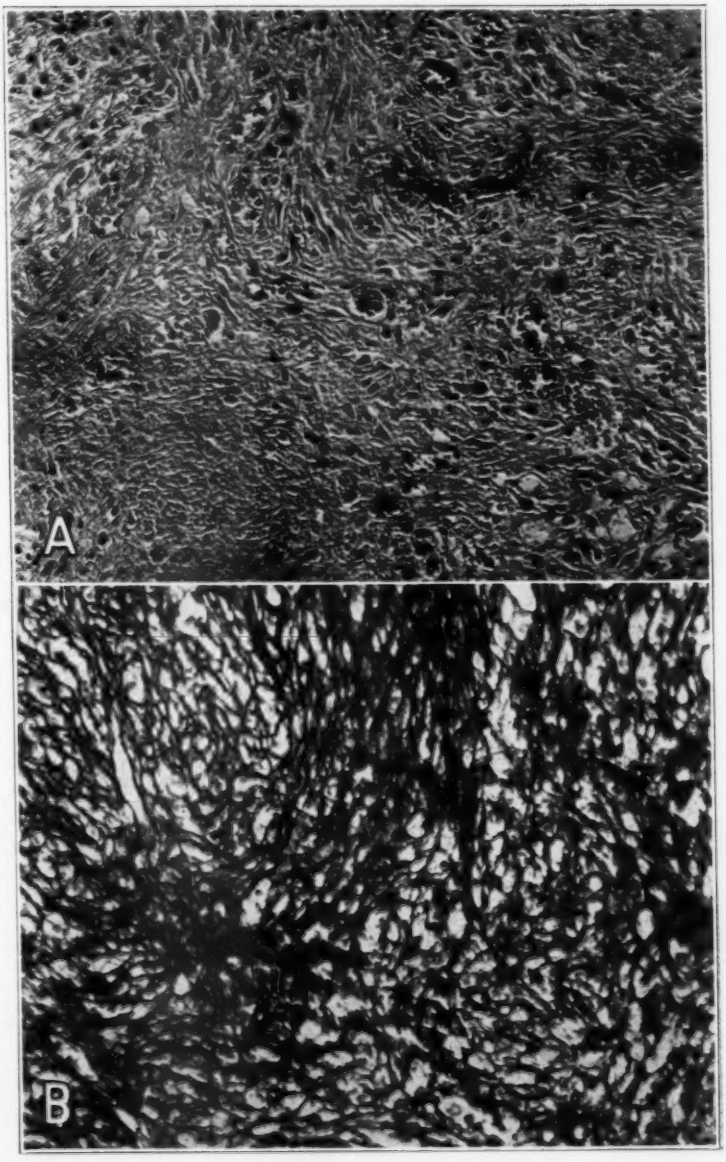

Fig. 5.—*A*, photomicrograph revealing an area of necrosis in the tumor (stained with hematoxylin and eosin). *B*, photomicrograph of the same area of necrosis reveals clearly the fibrils (stained with Laidlaw silver reagents).

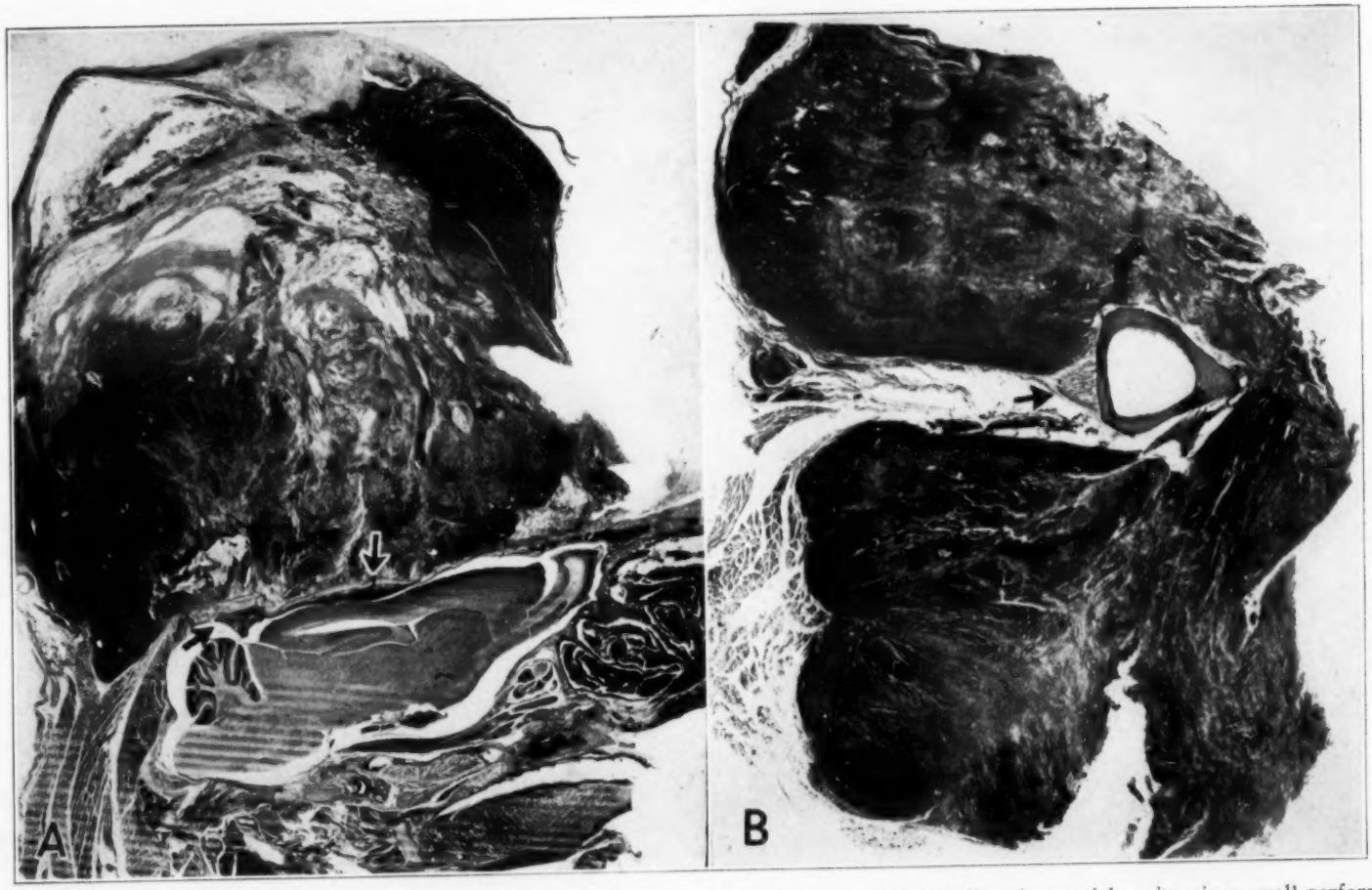

Fig. 6.—*A*, photomicrograph showing an enormous tumor situated on the calvarium. It is invading the cranial cavity via a small perforation in the calvarium (arrows). *B*, photomicrograph of a fibrosarcoma of the femur. Periostitis is present only where the tumor does not touch the cortex (arrow).

in the calvarium (arrows). *B*, photomicrograph of a fibrosarcoma of the femur. Periostitis is present only where the tumor does not touch the cortex (arrow).

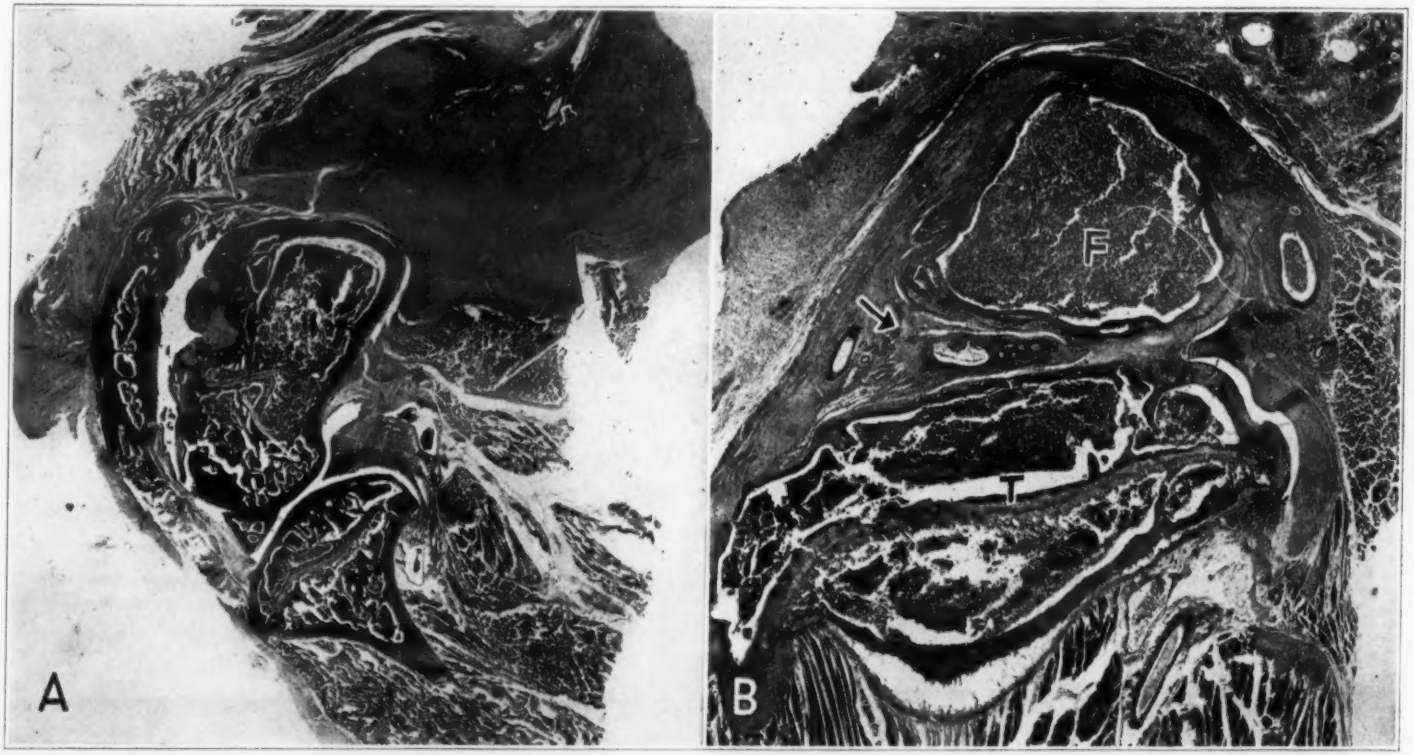

Fig. 7.—*A*, photomicrograph revealing that the tumor has entered the quadriceps pouch of the knee joint. The posterior capsule is also being invaded by tumor (fig. 1*A*). *B*, photomicrograph showing fibrous ankylosis of the knee, secondary to invasion of the capsule by tumor tissue (arrow). *F*, the femur; *T*, the tibia.

Fig. 8.—Photomicrograph showing the fibrosarcoma entirely replacing the bones in the knee joint. It spared only the distal epiphysial plate of the femur (arrow). Compare with figure *2 C*.

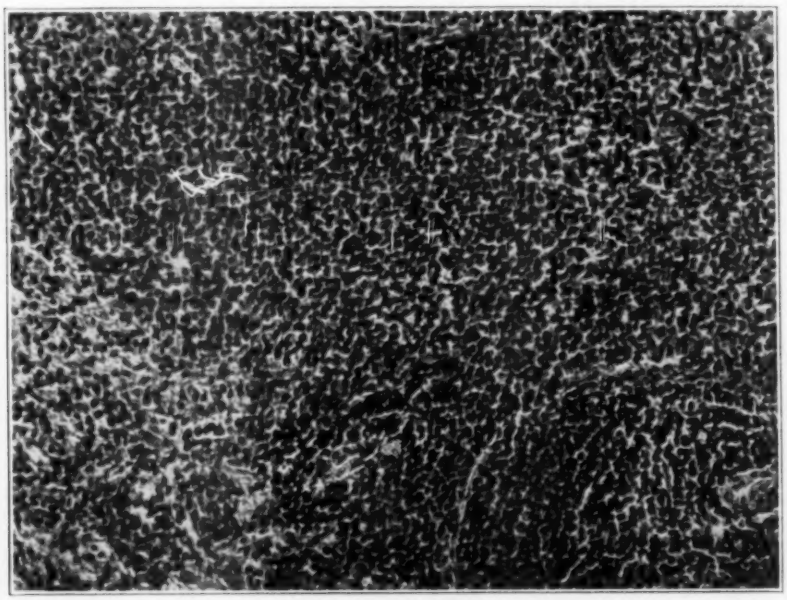

Fig. 9.—Photomicrograph showing a definite reticulum cell hyperplasia in the spleen of a rat sixty-eight days after the subcutaneous injection of 2 cc. of dibenzanthracene in lard.

When the Laidlaw silver reagents were used in histologic examination of the tumors, many of the tumor cells (especially those of the multinucleated type and also some of those in the myxomatous areas) proved to be "silver positive." The intercellular material of the tumors usually showed few fibrils. It was interesting to note, however, that in certain areas where early necrosis was in evidence and where the hematoxylin and eosin stains failed to bring out clearly the outlines of the cells and the fibrils of the matrix, the Laidlaw silver reagents revealed these plainly, occasionally also revealing the nuclei of the cells (figs. 4 and 5).

It may be assumed that those cells which showed positive staining in response to the presence of Laidlaw reagents represented still undifferentiated mesenchyme and were similar to bone marrow cells in their manner of reaction.[7]

The amount of periosteal reaction revealed by histologic examination of the skeletal tissues was minimal. Even when the tumor lay against the outer lamelli of the cortex, new bone formation was not a salient feature. However, in some cases the sarcoma did invade the contiguous bone and joints to some extent. In 1 animal the tumor invaded the posterior capsule of the knee, penetrating into the articular cartilage and inducing slight proliferation of the new bone on the tendon surface of the patella. In another rat the tumor attached itself to the paraarticular surface of the knee capsule. The knee joint underwent fibrous ankylosis (figs. 6 and 7).

Intra-articular injection of dibenzanthracene resulted in the development of a sarcoma which invaded most of the structures of the knee joint and partially replaced the crucial ligaments, the semilunar cartilages and the synovial linings. In addition, the tumor extended into the marrow cavity at the distal end of the femur.

Even the implantation of dibenzanthracene by surgical means into the marrow of the tibia did not produce an osteogenic tumor. It did, however, produce in 1 rat an invasive tumor which destroyed the entire lower end of the femur with the exception of its distal epiphysial plate (fig. 8). In another rat of this group a metastatic carcinoma was found in the tibia, just at the site of implantation of the anthracene. The primary tumor in this case was in the intestine.

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7. Laidlaw stated that cellular elements derived from the entoderm and ectoderm as well as those from hemopoietic, lymphatic and reticuloendothelial cells are "black-positive" in their staining reaction, while all other elements are "black-negative."

This was the only case in the entire series in which there was evidence of metastasis. On the other hand, most of the spleens, especially those of the tumor-bearing rats, showed definite hyperplasia of reticulum cells (fig. 9). The hemopoietic cells were also hyperplastic.

When examined with the aid of fluorescent microscopic technic many of the tumors revealed golden yellowish areas, usually in or near the cysts. This was not a constant finding, however, especially in rats which had had tumors for longer than twelve months after the initial

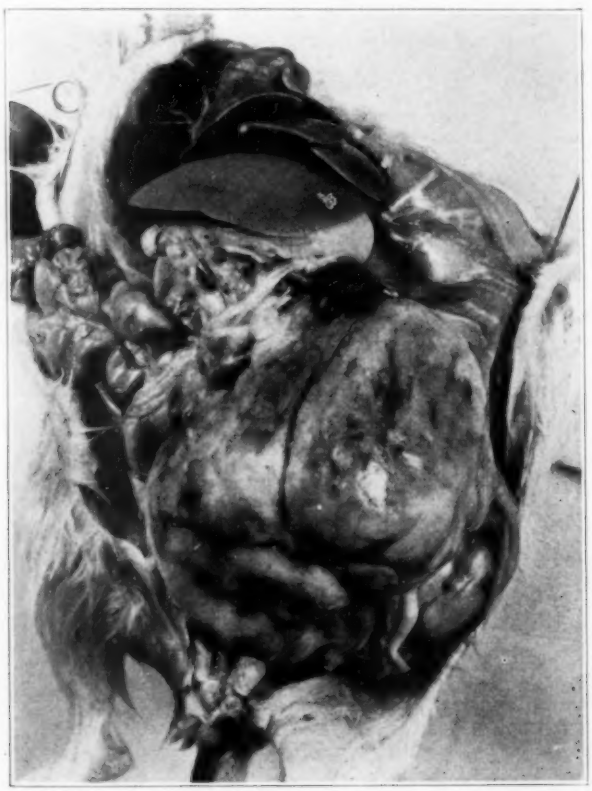

Fig. 10.—Large retroperitoneal sarcoma which encased the vertebral column (group E).

injection. Organs of the tumor-bearing rats and those without tumors were examined in the same way as the growths themselves, but no fluorescent areas were found.

COMPLICATIONS

Para-articular Ossification.—In 5 rats the injection of dibenzanthracene into the region of the lower lumbar vertebrae resulted in a large tumor. While the tumor did infiltrate the bony laminas (figs. 10

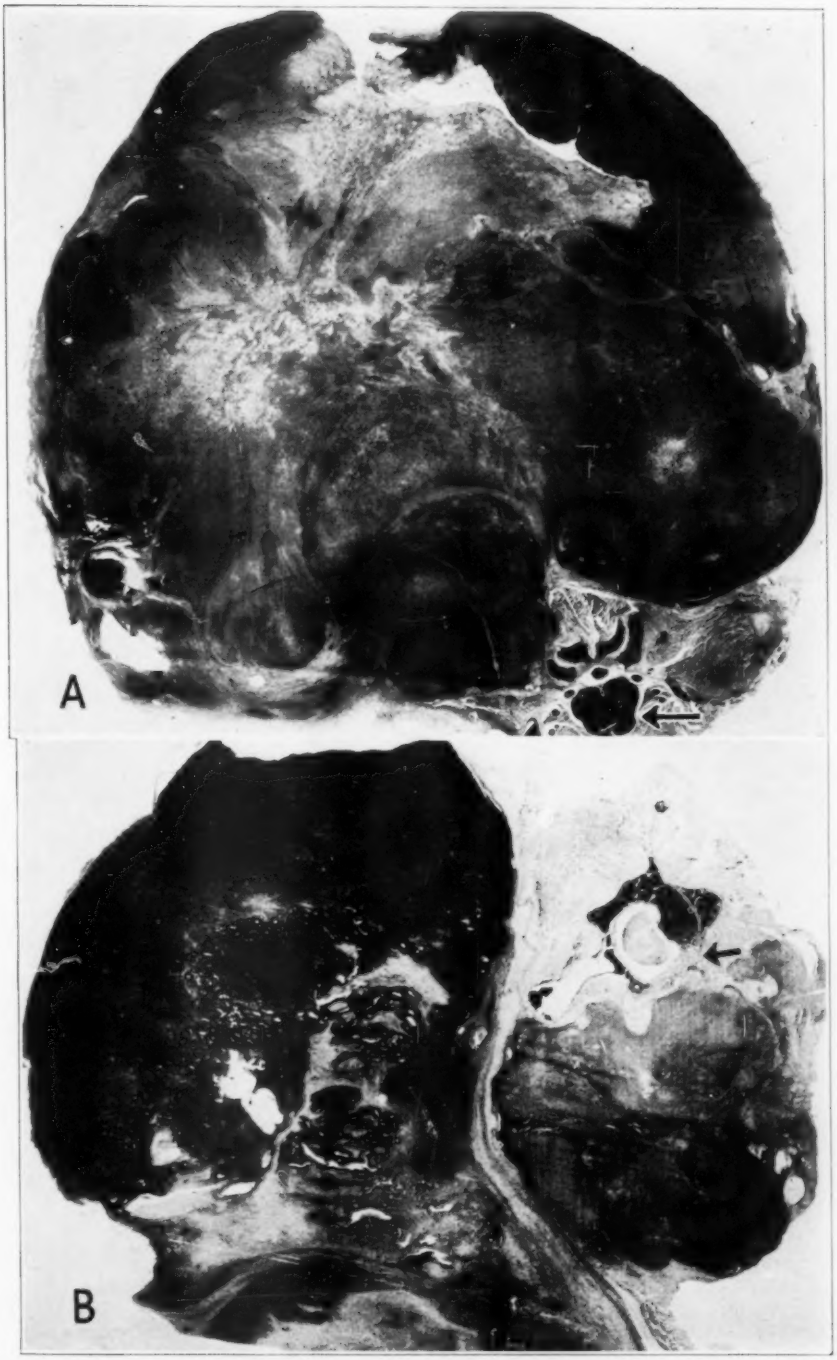

Fig. 11.—*A*, photomicrograph of another tumor in the same group, showing the relative location of the mass with reference to the vertebral column. The arrow points to the body of the lumbar vertebra. *B*, photomicrograph of the same tumor at another level, showing invasion into the lamina (arrow).

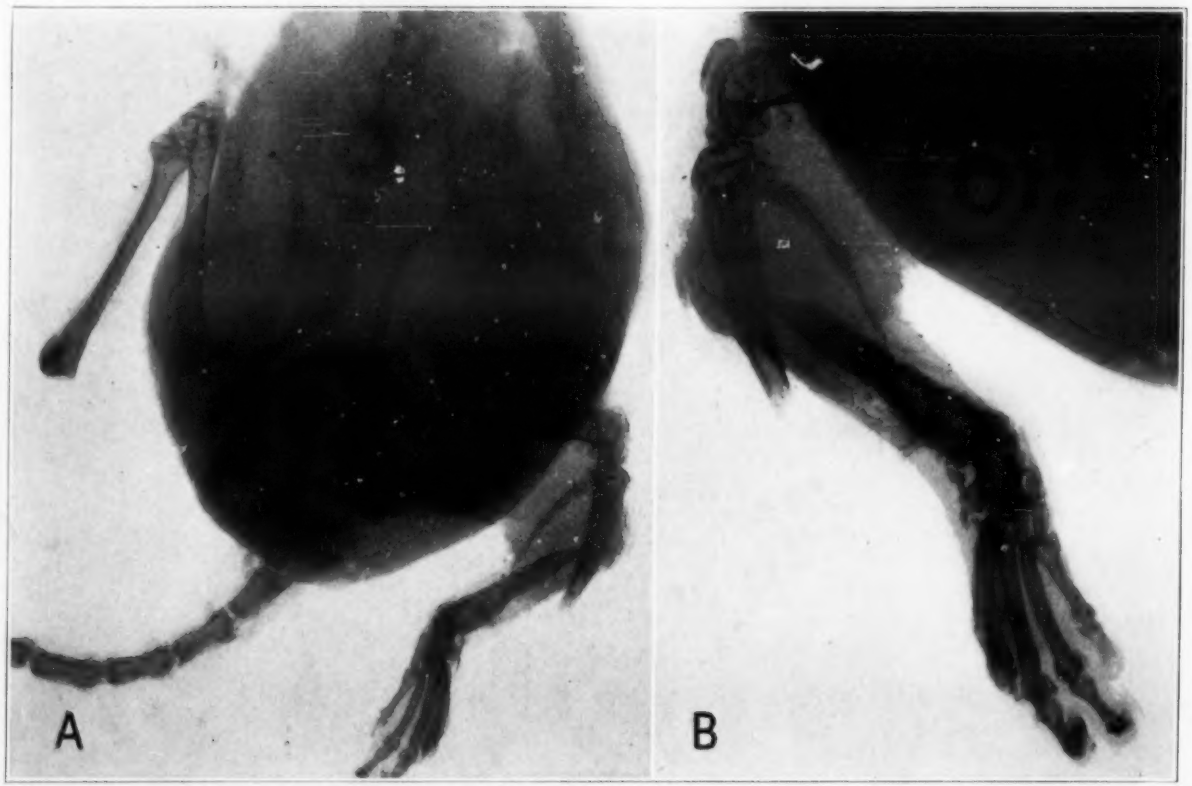

Fig. 12.—*A*, roentgenogram of tumor of the soft tissues in the lumbar portion of the vertebral column. Note the fracture and nonunion of the right tibia as well as the para-articular ossifications in the region of the right ankle. Periostitis and loss of some of the digits are also present. Spontaneous amputation above the ankle joint is noted in the opposite limb. *B*, enlargement of the roentgenogram of the right leg (fig. 12 *A*), revealing clearly the periostitis of the tibia and of the metatarsal bone. Note the para-articular ossifications.

revealing clearly the periostitis of the tibia and of the metatarsal bone. Note the para-articular ossifications.

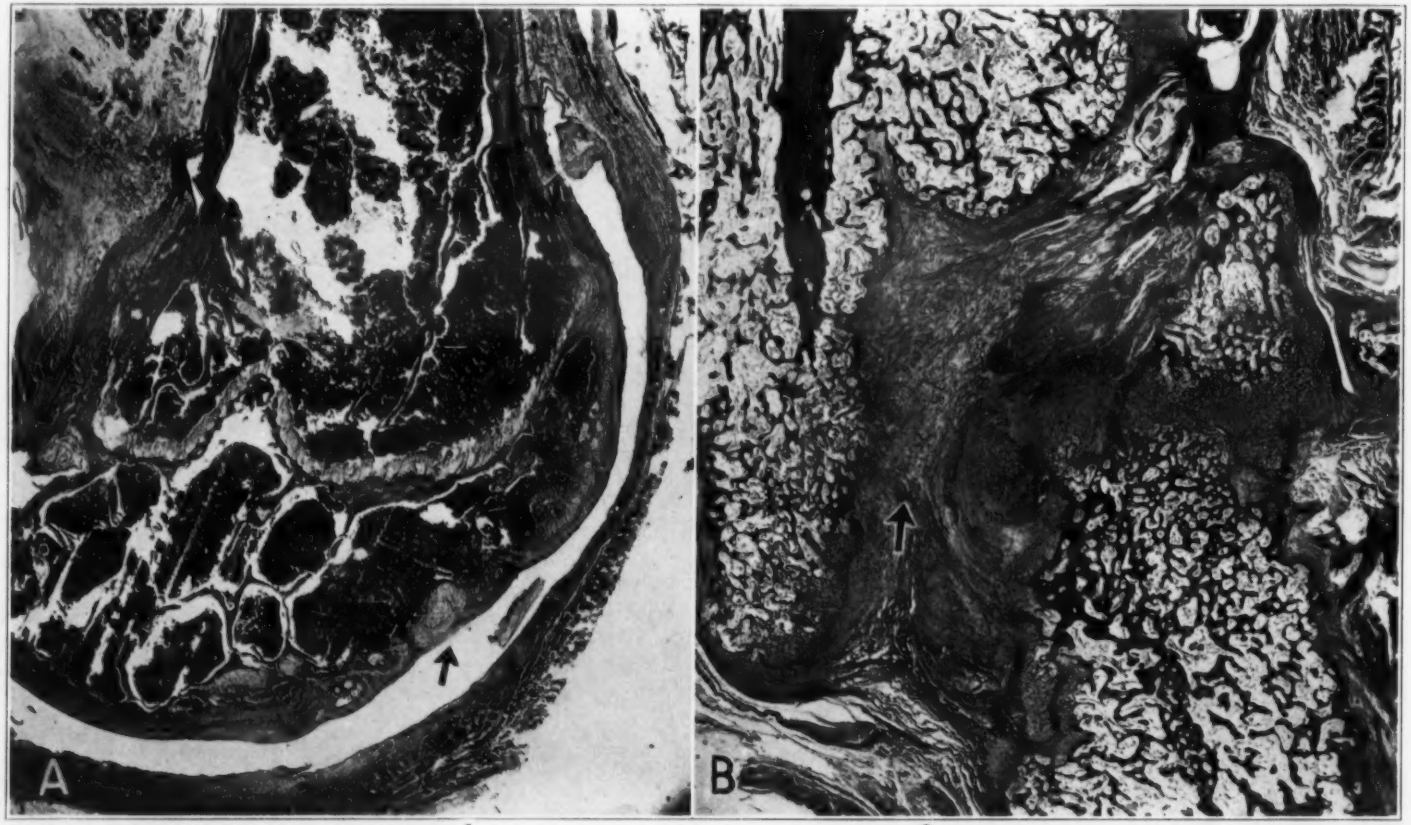

Fig. 13.—*A*, photomicrograph of the articular end of the left femur (same side as stump in figure 12 *A*), revealing definite arthritic manifestations, probably of neurotrophic origin. *B*, photomicrograph showing fibrous union of the fractured tibia in another rat in group E.

and 11), there was no case in which it invaded the spinal cord. The tumor-bearing animals showed gradually increasing paresis of the lower limbs. In 1 tumor-bearing rat the roentgenogram showed absence of several toes on the right foot, evidences of periostitis in one of the metatarsal bones and several para-articular ossifications in the region of the right ankle joint (figs. 12 and 13). Furthermore, it could be noted that the fracture of the right tibia had failed to unite. The other leg revealed a healed stump above the ankle, subsequent to a spontaneous amputation. The left knee joint showed definite arthritic

Fig. 14.—Photograph of a sarcoma invading the wall of the chest (arrow).

changes on microscopic examination. In another animal also, with a tumor in the lower vertebral column, nonunion of a fractured tibia was noted. These findings strongly suggest that the tumor produced a neurotrophic disturbance with secondary skeletal changes, analogous with that found clinically in cases of tabes dorsalis or transverse myelitis.[8]

Hypertrophic Periosteal Osteophytosis.—In another series of rats, in which dibenzanthracene was injected into the posterior aspect of the right scapula, 1 rat had a tumor about as large as a plum. The mass extended across the axilla and was attached to the humerus, the ribs

8. Corbin, K. B.: Alterations in the Hip Joint After Deafferentation, Arch. Surg. **35**:1145 (Dec.) 1937.

and the lungs (fig. 14). On histologic examination the cortex of the femur as well as that of the phalanges of the toes revealed evidence of definite increase in the number of outer lamellas, as shown by the cement lines. This is interesting as a possible indication of early hypertrophic periosteal osteophytosis. Further work along these lines is being done.[9]

SUMMARY

In this study, experimentally induced sarcoma, even when growing in tissues contiguous to skeletal parts, did not show any strong tendency to invade the skeleton. Even when a tumor was produced in the skeleton it was not an osteogenic sarcoma. (It should be noted, however, that 1 instance has been reported in which an osteogenic sarcoma was induced by dibenzanthracene.[2]) When invasion into the skeletal system occurred, it was by way of the capsule, as in relation to the knee joint; sometimes by way of the sutures, in relation to the calvarium, and less commonly by direct resorption of the cortex. Even when encased by an enormous tumor, however, the contiguous bone showed strikingly little periosteal reaction to the growth.

The presence of tumor in the vicinity of the spinal cord resulted in the formation of para-articular ossifications and skeletal abnormalities, which were interesting in that they simulated roentgenographically those sometimes noted in connection with neurotrophic disturbances in man.

In general, histologic examination of the tumors frequently showed it to be a mixed tumor containing elements to be found in fibrosarcoma, rhabdomyosarcoma and liposarcoma. In some of the neoplasms there were areas in which the tissue bore a striking resemblance to that of myxoma. When the Laidlaw silver stain was used, some of the nuclei in these areas, as well as nuclei apparently of the primitive types, stained "positive," and as a rule there was a concomitant sparsity of fibrils about such nuclei.

In both macroscopic and microscopic examination of the tumors and organs, filtered ultraviolet radiation was used to help establish qualitatively the presence or absence of the fluorescent drug dibenzanthracene. However, no residue of the drug could be detected in any of the organs, although it was revealed in the growths.

9. Compere, E. L.; Adams, W. E., and Compere, C. L.: Generalized Hypertrophic Pulmonary Osteo-Arthropathy, Surg., Gynec. & Obst. **61**:312 (Sept.) 1935.

SIXTY-EIGHTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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(Concluded from page 978)

MISCELLANEOUS

Roentgen Therapy in Acute Osteoporosis.—Osteoporosis is defined by Mumford [34] as that condition of bone which follows demineralization or absorption of the mineral salts of the bone. It is demonstrated by a thinning of the bone shadow in the roentgenogram. The author feels that osteoporosis should be classified as symptomatic or asymptomatic. The type with symptoms (the acute bone atrophy of Sudeck) responded to roentgen therapy in 5 of 6 cases. Roentgen therapy is administered in such dosage that erythema and burns will not occur.

Peritendinitis Calcarea.—Sandstrom [35] reports the results of roentgen treatment of calcaneous deposits in tendons, muscle and connective tissue in 329 cases. The deposits were located in the neighborhood of the shoulder, elbow, hip and knee joints, wrist, fingers and toes. He also reports on pathologic specimens obtained in 13 cases. In a number of conditions which are commonly classified as subdeltoid bursitis satisfactory therapeutic results were obtained with roentgen treatment.

Orthostatic Albuminuria.—According to Becher,[36] orthostatic albuminuria is best called lordotic albuminuria, because lordosis is the cause of the lesion. Investigations by Jekle have indicated that lordosis leads

34. Mumford, E. B.: J. Bone & Joint Surg. **20**:949, 1938.

35. Sandstrom, C.: Am. J. Roentgenol. **40**:1, 1938.

36. Becher, E.: Med. Klin. **34**:392, 1938.

to interference with the inferior vena cava. The consequent congestion of the veins of the kidney results in passage of serum albumin into the urine and acidosis. Administration of alkali will diminish lordotic albuminuria or stop it. Lordosis produced even in the supine position will cause albumin to pass into the urine in these patients. No damage to the kidneys even occurs as a consequence of recurring albuminuria. The condition is ameliorated by exercise, psychic treatment and military service.

[EDITORIAL NOTE.—One of the editors has followed a large group of children with this condition for a number of years. The albuminuria can be stopped when the lordosis, which frequently involves the lower dorsal part of the spine, is corrected. The response to treatment is prompt. If albuminuria continues after correction of lordosis, early nephritis will usually be found.]

Gas Gangrene.—The data obtained from vital statistics and from a survey of hospitals in the state of New York (exclusive of the city of New York) were studied by Bryant and Chapman.[37] They used the data for the years 1932 to 1936 inclusive. Two hundred and eight cases of gas gangrene were reported. One hundred and thirty-five of the patients were given an antitoxin for gas gangrene. Of 9 who received only a prophylactic dose of this serum, 2 died. Of 84 who received therapeutic doses, 29 died. Of 51 who received no serum, 35 died. These figures are not wholly correct, since a number of patients died from the disease which preceded the gas gangrene. The authors' statistics suggest that infection with the gas bacillus is as common as tetanus.

FRACTURES AND DISLOCATIONS

Treatment of Injuries of the Cervical Part of the Spine.—Forty-three patients with recent and old fracture-dislocations of the cervical part of the spine were treated by Crutchfield,[38] who uses a special instrument consisting of very small tongs for skeletal traction on the skull, held in place by a set screw. The tongs are applied through small stab wounds on either side, just large enough to admit the drill guard, which is drilled in for a distance of 3 mm. in children and 4 mm. in adults. The fixed guard prevents excessive penetration. The points of the tongs are fitted into the bone perforations and held in position until the tongs have been locked. Of the 43 patients treated, 14 died as the result of damage to the spinal cord and associated injuries. Twenty-nine cases, therefore, were analyzed for this report. The advantages of this method of treatment are numerous; headache and other disagreeable symptoms are

37. Bryant, T. L., and Chapman, O. D.: New York State J. Med. **38**:696, 1938.
38. Crutchfield, W. G.: J. Bone & Joint Surg. **20**:696, 1938.

eliminated, the care of the skin is much easier, and the patient is allowed more freedom of movement. The author has never used traction of more than 25 pounds (11.3 Kg.). In recent cases of injury to this portion of the spine, reduction has been accomplished usually within a few minutes. By the application of efficient, properly directed traction the danger of increasing deformity is eliminated. Reduction, immobilization in plaster and removal of the tongs, all within a few hours, are carried out on patients who are able to stand such treatment, but most of the author's patients were too ill for immediate immobilization. In most cases he applied traction at once and on the following morning made a roentgenologic examination. If reduction had been accomplished and there was little or no injury to the cord, immobilization in plaster was carried out at once. Patients with injured spinal cords were kept in light traction, 4 to 6 pounds (1.8 to 2.7 Kg.) being applied, until they passed the critical ten day period. The author uses traction of 25 pounds (11.3 Kg.) for dislocations in the middle third of the cervical spine; in the upper third only 10 to 15 pounds (4.5 to 6.8 Kg.) is necessary. Excellent illustrations accompany the next.

Injury to the Spinal Cord During Reduction of Fractures of the Vertebrae.—Of 70 patients with fracture and dislocation of the thoracic and lumbar vertebral bodies treated by Rogers [39] in the past nine years, only 2 showed fracture dislocations and 2 showed crush fractures involving the posterior wall of the centrum with backward displacement of the bone fragments. In none of these 4 cases was there any evidence of injury to the cord or pressure on the nerve roots immediately after the injury. In 3 cases paralysis developed as a result of treatment: in 2 cases of fracture dislocation during reduction and in 1 case of vertebral fracture two years after injury. In none of the other 66 cases, in which the usual wedge compression was present, was there slightest evidence of pressure on the spinal cord or the nerve roots incident to treatment. The author groups all fractures of the vertebral bodies, therefore, into two groups, the "safe" group, in which the fracture does not involve the posterior wall of the centrum (this represents 90 per cent) and the "dangerous" group, which includes all dislocations and all fractures involving the posterior wall of the centrum. It is essential, therefore, that the alinement of the articular processes be determined accurately before reduction is attempted. If there is lateral disalinement, the reduction should be open and flexion should be employed to disengage the locked processes. Extension of the spine in such a case may injure the cord or the nerve roots. Traction alone will not free locked articular processes.

39. Rogers, W. A.: J. Bone & Joint Surg. **20**:689, 1938.

Postural Reduction of Fractures of the Spine.—Watson-Jones [40] feels that in reduction of fractures of the spine, hyperextension to the normal limit is necessary. This position varies considerably in different patients. Therefore he feels that controlled degrees of extension by slings or curved surfaces are imperfect. Instead the trunk should be entirely unsupported, so that it sags into space to the limit of the patient's movement in extension. The patient rests on two tables in such a way that his abdomen sags between the two. The legs and about three fourths of the thighs rest on the lower table and about two thirds of the upper parts of the arms remain on the upper table. The author feels that if more of the body is supported by the table than this the spine cannot sag sufficiently to give complete extension. He reports a series of 252 fractures of the spine and classifies them into three groups, namely, simple wedge fracture, comminuted fracture and fracture dislocation. The simple wedge fracture is the most common and is due to falling from a height and landing on the heels or the buttocks. Often the intervertebral disks are uninjured, and spontaneous ankylosis is rare. The comminuted fracture is the next most common and is caused by forcible acute angulation. The intervertebral disks are ruptured, and bony ankylosis is common. Fracture dislocation is due to the fall of a weight on the shoulders, and the spinal cord is usually injured. In the wedge and comminuted types of fracture excellent anatomic results are obtainable by the postural method of treatment. Eighty per cent of the patients resume their original occupation; the average period of disability is ten months. In cases of fracture dislocation, immobilization and extension are advisable. Laminectomy is not advisable. The prognosis is bad for high thoracic dislocations with paraplegia, fair for cervical injuries and good for lumbar injuries. The author lists common sources of failure as follows: Uncorrected wedging causes persistent pain due to interarticular joint strain. Neglect of finer details of the technic of postural reduction causes failure. The jacket must not be cut below the clavicle or above the groin; the cutting of an abdominal window is not advisable. Early manipulation is safe. The jacket must be renewed every two weeks. The patient must be immobilized for from four to six weeks. Posterior spinal splints are not advisable. Two hyperextension fractures are reported. One was a fracture of the vertebral body, and the other was a fracture of the pedicle. A fracture dislocation with locking of the articular processes can be treated only after one, and frequently both, articular processes have been excised.

40 Watson-Jones, R.: J. Bone & Joint Surg. **20**:567, 1938.

Recurrent Dislocation of the Shoulder.—Bankhart [41] points out that ordinary dislocation of the shoulder and recurrent dislocation are entirely different injuries. The former is caused by a fall on the abducted arm, levering the head of the humerus out through the inferior part of the capsule, which heals readily after reduction. The latter injury is caused by a fall on the back of the shoulder or on an elbow directed backward, which forces the head of the humerus forward and shears off the fibrocartilaginous glenoid ligament from its attachment to the bone. There is no tendency for this ligament to reattach itself to the bone, so the defect is permanent. The author has exposed this lesion at operation in 27 consecutive cases of recurrent dislocation. The exposure is made by approaching between the deltoid and pectoralis major muscles. The coracoid process is divided by an osteotome and pulled downward. The tendon of the subscapularis muscle is exposed and divided, exposing the joint capsule. The periosteum is raised over the anterior aspect of the neck of the scapula, and the joint capsule is sutured to the bare bone thus exposed. In all the author's 27 cases full movement of the joint was recovered, and there was no recurrence of dislocation.

Excision of Ununited Scaphoid Bone.—Davidson and Horwitz [42] removed the carpal scaphoid bone from 8 patients in whom nonunion persisted after fracture; in 7 the excision of the scaphoid was complete, and in 1 it was partial. The end results in 5 instances were good, the patients returning to their former work. There was slight radial deviation in 2 instances. In 2 patients with nonunion of two years' duration the end result was good but there was considerable osteoarthritis. In 1 patient who had nonunion of seven years' duration there was much pain and osteoarthritis. The authors feel that excision should be done early when nonunion is present, before secondary arthritic changes have taken place.

Pseudarthrosis of the Tibia.—Hallock [43] states that in the past two methods of repair have been used chiefly in treatment of pseudarthrosis, namely, open reduction and massive graft. These measures, he states, have often been ineffective, especially in pseudarthroses of congenital origin and in children under 12. The author's technic consists in exposing the area of pseudarthrosis by subperiosteal dissection. The ends of bone are freshened or resected in sufficient amount to correct existing deformity and are placed end to end if possible. A broad, shallow longitudinal groove is fashioned in both fragments, extend-

41. Bankhart, A. S. B.: Brit. J. Surg. **26**:23, 1938.

42. Davidson, A. J., and Horwitz, M. T.: Ann. Surg. **108**:291, 1938.

43. Hallock, H.: J. Bone & Joint Surg. **20**:648, 1938.

ing from good bone in the upper fragment to good bone in the lower fragment. The groove is then filled with many small bone transplants or chips taken from the opposite tibia or from the ilium. The periosteum is closed with interrupted sutures, and the procedure is carried out under a tourniquet. Walking in the cast is usually allowed ten to twelve weeks after operation, at which time the cast is first changed. Immobilization in plaster is maintained until the roentgenogram shows sufficient new bone to permit function without support. The author feels that by this procedure adequate reparative growth of granulation tissue is promoted and that the ununited fragments are brought into extensive contact through the medium of many small bone masses which will quickly and readily become recalcified and rehabilitated. He has performed 7 primary and 4 secondary multiple bone transplant operations for 7 pseudarthroses. In 3 of the secondary operations a large graft was used in addition to the chips, chiefly for purposes of immobilization. Of the 7 primary operations, 4 succeeded and 3 failed. Excellent line drawings as well as roentgenograms illustrate the text.

Posterior Marginal Fractures of the Tibia.—D'Aubigne [44] offers a method of reduction of resistant trimalleolar fractures of the ankle. In these fractures it is usually the posterior marginal fracture of the tibia which is the chief obstacle to reduction. If the posterior marginal fracture involves a third of the articular surface the displacement is often irreducible; if it involves a half of the articular surface it is always irreducible, the posterior dislocation of the astragalus recurring as soon as the forward force is stopped. Open operation, which is commonly employed in the difficult cases, has several disadvantages. It may be impossible until very late because of excessive swelling and blisters. A large incision is necessary, with cutting of the achilles tendon. Accurate approximation of the posterior tibial fragment is difficult even by open operation. Lastly, the danger of infection is always present. The method of continuous traction by a pin in the os calcis is usually unsatisfactory, because reduction cannot be perfectly maintained. Consequently, the author has devised the following method: With the patient under general or spinal anesthesia, the leg is prepared with iodine and placed, with the knee flexed, on a Bohler reduction frame. Traction on the os calcis is established by a pin or a heavy wire, the force of the traction being obliquely upward and forward. A second pin is placed through the lower third of the tibia and is attached downward to the frame for counter-traction. By means of screwing up the traction on the os calcis, the fracture is reduced and

44. D'Aubigne, R. M.: J. de chir. **52**:168, 1938.

is checked by roentgenogram. In order to hold the reduction, a threaded steel pin is inserted, by means of a special three point guide, almost anteroposteriorly from the posterolateral border of the external malleolus, through the malleolus, to emerge through the tibia at its anteromedial part. Through small incisions, washers and nuts are placed on each end of the threaded pin, and the protruding ends of the pin are cut off and the wounds closed. The os calcis and tibial wires are then removed. A well molded plaster boot is applied, the foot being left free, and a walking iron is incorporated into the plaster. This technic has been used in 3 cases, with satisfactory results.

ORTHOPEDIC OPERATIONS

Operation for Paralysis of Intrinsic Muscles of Thumb.—Royle [45] describes an operation to restore the opposing function of the thumb when there is paralysis of the intrinsic thenar muscles. The flexor sublimis muscle to the ring finger is used. This muscle is divided just beyond its bifurcation at the base of the finger, drawn back and out at the wrist and then passed up the sheath of the long flexor of the thumb and attached one branch to the short flexor muscle and the other to the opponens pollicis. Reeducation is simple since attempting to flex the ring finger draws the thumb into opposition.

[EDITORIAL NOTE.—This operation seems simpler in technic than the other methods of tendon transplantation, most of which must utilize a tendinous pulley to secure pull in the correct direction.]

Spondylolisthesis.—Speed [46] describes a method of anterior fusion of the fifth lumbar vertebra to the sacrum by implantation of an autogenous bone graft through the body of the fifth lumbar vertebra, traversing its intervertebral disk into the upper sacral segment. This operation was performed for spondylolisthesis of the fifth lumbar vertebra. The patient was seen about six months after the operation. He was able to walk without support and complained of no pain in his back, though he still had some dragging sensation in the leg and tiring of the upper parts of the thighs after walking two blocks.

[EDITORIAL NOTE.—Most patients suffering from spondylolisthesis are relieved of their pain when a spinal support is properly fitted to the lower part of the back. In the opinion of the editors, so extensive an operative procedure as that just described is justifiable only when all conservative measures have failed.]

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45. Royle, N. D.: Operation for Paralysis of the Intrinsic Muscles of the Thumb, J. A. M. A. **111**:612 (Aug. 13) 1938.

46. Speed, K.: Spondylolisthesis: Treatment by Interior Bone Graft, Arch. Surg. **37**:175 (Aug.) 1938.

Fusion in Charcot's Disease of the Knee.—A single case of successful fusion of Charcot's knee joint was reported by Soto-Hall [47] in the hope that the technic used might be of value in lowering the high percentage of failures following operation for this disease. The author believed that failure of arthrodesis in these knees was the result of curtailment of the blood supply and sclerosis of the bones. Consequently he performed the arthrodesis in two stages. First the knee joint was exposed and multiple ¼ inch (0.6 cm.) drill holes were made in both the femur and the tibia. Five weeks later the joint was again opened and a fusion operation was performed, the bones being fixed with two Steinman pins. Union was obtained, and the patient walked without support after seven months.

Resection of the Proximal Phalanx of the Great Toe for Hallux Valgus.—Lindemann and Meyerhoff [48] report a seven year follow-up on a series of 104 operations of a total of 128 performed for hallux valgus. The procedure in each instance was that popularized by Brandes in 1928 and consisted of resection of two thirds of the basal phalanx and lengthening of the shortened extensor hallucis muscle. Fifty-two patients were completely free from pain and presented a cosmetically satisfactory great toe. In 40 cases the results were termed functionally satisfactory. However, there appeared in various members of this group mild pain, recurrent deviation of the toe, shortening of the toe and limited articular motion. In 12 cases in which treatment failed there was either stiffening of the metacarpophalangeal joint or recurrence of the hallux valgus. Only 2 patients of this group complained of pain. As a rule, the patient is well three or four weeks after operation. Physical therapy and supports are employed in the after-care.

Treatment of Severe Paralytic Calcaneus.—Tendon transplants have been employed by Leveuf and Bertrand [49] in all cases of paralytic calcaneus in spite of the theoretic objection that the substituted muscles are very weak compared with the gastrocnemius muscle. The deformity must be reduced before the transplant is done, and only muscles which have the function of plantar flexion should be used. The bony correction must fulfil two conditions: 1. The relations of the calcaneus with the forefoot must be reestablished, and the arm of the calcaneal lever must be elongated so that the transplanted muscles will work at a mechanical advantage. 2. The articulations which permit lateral motion must be fused so as to assure lateral stability and to permit all muscles to act only as flexors and extensors. In most cases, the operation on the bones and the tendons has been done at the same time. The incision curves

47. Soto-Hall, R.: Ann. Surg. **108**:129, 1938.

48. Lindemann, K., and Meyerhoff, M.: Ztschr. f. Orthop. **67**:36, 1938.

49. Leveuf, J., and Bertrand, J.: J. de chir. **52**:145, 1938.

around the external malleolus to end on the dorsum of the foot. The peroneal tendons are isolated and cut as far distal as possible. The midtarsal and subastragalar joints are next resected. The head and neck of the astragalus are excised to allow backward displacement of the calcaneus. A wedge-shaped resection of the subastragalar joint is done with the base posteriorly, most of the wedge being taken from the calcaneus. This allows correction of the os calcis. In order to correct the cavus fully, a plantar fasciotomy may be done, but overcorrection should be avoided. After this resection it is noted that the scaphoid forms an anterior block. In the tendon transplant all the flexor muscles can be utilized, but as a rule both peroneals and the tibialis posterior are the ones most frequently used. The flexor hallucis and flexor digitorum longus muscles should not ordinarily be used, since they are important for a good gait. The peroneus brevis muscle alone should not be transplanted, since the longus muscle will then increase the cavus. In the operation the tendons are cut as far distally as possible and are then passed through osseous tunnels on the posterosuperior aspect of the calcaneus. Reefing of the achilles tendon is done only when there is some power left in the muscle. The foot is immobilized in plaster for two months. Walking is permitted in three months, with use of a device to raise the heel.

Recurring Deformity in Stabilization of the Foot.—A series of consecutive stabilizations of the foot for correction of the deformities associated with residual poliomyelitis has been studied by Crego and McCarroll [50] with reference to recurrent deformities. They found that such recurrences were caused by some form of abnormal muscular control. They decided that in order to prevent such secondary manifestations it is essential that the muscular power on the medial and lateral aspects of the ankle joint be perfectly balanced or completely removed after arthrodesis. Because of the difficulty encountered in estimating the exact power of individual muscles, the peroneal and the posterior and anterior tibial muscles are now transplanted to the midline posteriorly or anteriorly, unless the muscles are known to be completely paralyzed. If transplantation is not needed it is better to excise the tendons thoroughly. The only exception to this is in case of a cavus deformity secondary to paralysis of the intrinsic muscles of the foot in which all the long muscles are known to be normal in power. Other etiologic factors associated with malformation are tibial torsion, knock knee and exaggerated bow in the lower thirds of the legs. The authors feel that in stabilization of any foot the foot should be placed in correct alinement with the malleoli of the ankle joint without regard to other deformities. Procedures necessary for the correction of other deformi-

50. Crego, C..H., and McCarroll, H. R.: J. Bone & Joint Surg. **20**:609, 1938.

ties are carried out at a later operation in order to establish a satisfactory line of weight bearing in the extremity as a whole. Four of the authors' cases showed recurrence as a result of stabilization formed at too early an age. Recurrence could have been prevented, the authors feel, by waiting until the child was 8 years old before performing the operation. After deformities have once recurred, they are corrected by restabilization of the foot, followed by removal or correction of the cause of recurrence.

RESEARCH

Chemical Composition of Voluntary Muscle.—Reinhold and Kingsley [51] studied the chemical composition of voluntary muscle obtained for biopsy from 12 patients suffering from muscular dystrophy and from 16 patients suffering from other muscular diseases. They found that the creatine concentration is lowered in the early stages of muscular dystrophy, before there is much muscular impairment. As the disease advances the creatine loss becomes greater. The total acid-soluble phosphorus content was also lowered in proportion. No change was observed in the results of chemical analysis after glycerin feeding for as long as twenty-two months. The histologic picture also remained the same. In myasthenia gravis there was a higher concentration of soluble ester phosphorus. In semistarvation the creatine content was lowered, as was the total acid-soluble phosphorus content. In myositis the changes were comparable to muscular dystrophy but were milder in degree. Less pronounced changes were observed in diseases of the nervous system. The authors state that chemical analysis of muscle is an aid in diagnosis and in estimating the degree of muscular deterioration.

Electrocoagulation of Osseous Tissues.—Zschau [52] reports on the electrocoagulation of bone, bone marrow, cartilage, periosteum and synovial membrane in guinea pigs. Bone is the most sensitive of these structures; cartilage is the least sensitive. When periosteum is destroyed by a strong coagulation current, it is replaced by fibrous tissue without osteoplastic power. Weak coagulation, on the other hand, excites bone formation. The synovial membrane was replaced by granulation tissue, which in a few weeks resembled the original synovial tissues.

Experimental Osteomyelitis in Rabbits.—Thompson and Dubos [53] in a study to test the virulence of various strains of Staphylococcus aureus found that they were able to produce osteomyelitis in rabbits. The virulence of the staphylococci was raised by their passage through the animal species. In further studies on 31 rabbits 2 months old 18 were found to have osseous lesions after intravenous injections of

51. Reinhold, J. G., and Kingsley, G. R.: J. Clin. Investigation **17**:377, 1938.
52. Zschau, H. D.: Ztschr. f. Chir. **250**:89, 1938.
53. Thompson, R. H. S., and Dubos, R. J.: J. Exper. Med. **68**:191, 1938.

staphylococci. Nine of the animals died from general infection in too short a period for the development of osseous lesions. Fifty-five lesions were observed in the bones of the 18 rabbits. Forty-seven of these lesions were at the ends of the long bones. Serous effusions into neighboring joints were commonly observed, but purulent arthritis occurred in only 8 instances. The microscopic appearance of the osseous lesions was similar to that of osteomyelitic lesions in man.

[EDITORIAL NOTE.—This interesting study suggests that blood-borne infection lodges much more frequently in bones than in joints. It offers a possible experimental approach to therapeutic endeavors which could eventually be applied to human osteomyelitis.]

Hereditary Bone Tumors in Mice.—Pybus and Miller [54] obtained 260 bone tumors, chiefly sarcomas, in mice from an inbred strain. These tumors developed in a cancer-producing strain of mice. The authors have been able to secure an incidence of 10 per cent of bone tumors. The most common sites of the lesions were the femur, the tibia and the spine. Histologically the authors were able to study tumors from the earliest proliferation of osteoblasts to all gradations of differentiation and malignancy. They feel that further study of this strain of mice may help in solving some of the problems presented by bone tumors in man.

Osseous Lesions in Experimental Scurvy.—Ham and Elliott [55] produced protracted moderate scurvy in young guinea pigs by feeding them diets containing less than adequate amounts of vitamin C. Longitudinal growth of bone continued in the peripheral part of the epiphysial plate and in the ring of diaphysis adjacent to the periphery of the plate. In the epiphysis a diminution in the amount of bone supporting the articular cartilage was found. The authors suggest that certain features of osteoarthritis may be the effect of a long-continued moderate deficiency of vitamin C.

54. Pybus, E. C., and Miller, E. W.: Brit. M. J. **1**:1300, 1938.
55. Ham, A. W., and Elliott, H. C.: Am. J. Path. **14**:323, 1938.

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